

Guidelines for

ATC classification

and **DDD** assignment

2011



WHO Collaborating Centre for
Drug Statistics Methodology



Norwegian Institute of Public Health

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and DDD assignment
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Guidelines for ATC classification and DDD assignment

14th edition

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PREFACE

The Anatomical Therapeutic Chemical (ATC) classification system and the Defined Daily Dose (DDD) as a measuring unit are recommended by the WHO for drug utilization studies. The system is now widely used internationally and the number of users is gradually increasing. The purpose of preparing guidelines is to make information about the ATC classification system and the DDD methodology available to the users.

The members of the WHO International Working Group for Drug Statistics Methodology have given expert advice and comments on the work with these guidelines.

This 14th edition of the *Guidelines for ATC classification and DDD assignment* is based on the ATC classification index with DDDs valid from January 2011. The ATC index with DDDs, which is important for the understanding of these guidelines, is available on request from the WHO Collaborating Centre for Drug Statistics Methodology (order form, see Annex II). A searchable version of the index is available on our website www.whocc.no. The ATC index with DDDs is updated annually. Please be aware that Spanish versions of the ATC/DDD publications also are available.

An integrated version of the *Guidelines for ATC classification and DDD assignment* and *ATC classification index with DDDs* is available on internet. For further information, please see our website: www.whocc.no.

All comments connected to the assignment of DDDs are given in shadowed boxes in the various chapters to each ATC group.

We hope this book will prove helpful to the users of the ATC/DDD system. Suggested improvements can be addressed to the WHO Centre in Oslo.

Oslo, December 2010
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I. INTRODUCTION

A. History of the ATC/DDD system

The field of drug utilization research has attracted increasing interest since its infancy in the 1960s. The pioneering work was done by two consultants at the WHO Regional Office for Europe, Engel and Siderius (The consumption of drugs: report of a study 1966-1967. WHO regional Office for Europe, 1968). Their study of drug consumption in six European countries during the period 1966-1967 showed great differences in drug utilization between population groups. This study was followed by a symposium in Oslo in 1969 entitled *The Consumption of Drugs*, organised by the WHO Regional Office for Europe. It was agreed at this symposium that an internationally accepted classification system for drug consumption studies was needed. It was also at this symposium that the Drug Utilization Research Group (DURG) was established and tasked with the development of internationally applicable methods for drug utilization research.

By modifying and extending the European Pharmaceutical Market Research Association (EphMRA) classification system, Norwegian researchers developed a system known as the Anatomical Therapeutic Chemical (ATC) classification.

In order to measure drug use, it is important to have both a classification system and a unit of measurement. To deal with the objections against traditional units of measurement, a technical unit of measurement called the Defined Daily Dose (DDD) to be used in drug utilization studies was developed. The ATC/DDD system has been used in Norway since the early seventies for presenting drug consumption data.

The Nordic Council on Medicines (NLN) established in 1975, collaborated with Norwegian researchers to further develop the ATC/DDD system. The NLN published the Nordic Statistics on Medicines using the ATC/DDD methodology for the first time in 1976. Since that time the ATC/DDD system has expanded to include most drugs on the Nordic market. At the same time, international interest in the ATC/DDD system for drug utilization research expanded beyond the Nordic countries largely through the activities of the DURG who recommended the ATC/DDD methodology for international drug utilization studies.

B. Present Organisational responsibility for the ATC/DDD system

1. WHO Collaborating Centre for Drug Statistics Methodology

In 1981, the WHO Regional Office for Europe recommended the ATC/DDD system for international drug utilization studies. In connection with this, and to make the methodology more widely used, there was a need for a central body responsible for coordinating the use of the methodology. *The WHO Collaborating Centre for Drug Statistics Methodology* was accordingly established in Oslo in 1982. The Centre was until 2001 situated at the Norwegian Medicinal Depot (NMD). From January 2002 the Centre has been located at the Norwegian Institute of Public Health. The Centre is funded by the Norwegian government.

In 1996, WHO recognized the need to develop use of the ATC/DDD system as an international standard for drug utilization studies. The Centre was therefore linked directly to WHO Headquarters in Geneva instead of the WHO Regional Office for Europe in Copenhagen. This was seen as important to allow close integration of international drug utilization studies and WHO's initiatives to achieve universal access to needed drugs and rational use of drugs particularly in developing countries. Access to standardised and validated information on drug use is essential to allow audit of patterns of drug utilization, identification of problems, educational or other interventions and monitoring of the outcomes of the interventions.

An Agreement was drawn up by WHO with the Government of Norway in 1996 and revised in 2002. The latest redesignation of the Department of Pharmacoepidemiology, Norwegian Institute of Public Health, as a WHO Collaborating Centre for Drug Statistics Methodology, was in May 2008. According to this Agreement all activities related to ATC/DDD classification have to be conducted in accordance with policies determined by WHO.

The main activities of the Centre are development and maintenance of the ATC/DDD system, including:

- To classify drugs according to the ATC system.
- To establish DDDs for drugs which have been assigned an ATC code.
- To review and revise as necessary the ATC classification system and DDDs.
- To stimulate and influence the practical use of the ATC system by cooperating with researchers in the drug utilization field.

- To organize training courses in the ATC/DDD methodology and to lecture such courses and seminars organized by others.
- To provide technical support to countries in setting up their national medicines classification systems and build capacity in the use of medicines consumption information.

2. WHO International Working Group for Drug Statistics Methodology

In 1996, when the decision on globalizing the ATC/DDD system was taken, the WHO Division of Drug Management and Policies established *the WHO International Working Group for Drug Statistics Methodology*. The International Working Group comprises 12 members drawn from the WHO Expert Advisory Panels for Drug Evaluation and for Drug Policies and Management. The International Working Group members are selected by WHO Headquarters to represent a wide range of geographical and professional backgrounds, including clinical pharmacology, clinical medicine, international public health, drug utilization and drug regulation. The members of the International Working Group represent different users of the ATC/DDD system and different nationalities as they represent the 6 WHO global regions. The WHO Collaborating Centre for Drug Statistics Methodology receives expert advice from the Working Group.

The main terms of reference of the Working Group are:

- To continue the scientific development of the ATC/DDD system.
- To discuss and approve all new ATC codes, DDD assignments and alterations to existing ATC codes and DDDs.
- To develop further the use of the ATC/DDD system as an international standard for drug utilization studies.
- To revise as necessary the guidelines for assignment and change of ATC codes and DDDs.
- To revise as necessary the procedures for applications for assignment of and changes to ATC codes and DDDs to ensure they are consistent and transparent.
- To assess the sources and availability of statistics on drug use internationally, and to encourage the systematic collection of comprehensive drug use statistics in all countries and regions using the ATC/DDD system as the international standard.

- To develop methods, manuals and guidelines for the practical application and appropriate use of the ATC/DDD system in drug utilization studies in a variety of settings, particularly those applicable to developing countries.
- To work with groups involved in rational drug use initiatives to integrate methods for measurement of drug use in assessing needs and outcomes of interventions with the aim of improving drug use.

The International Working Group meets twice annually. A teleconference may replace one of the two annual meetings.

Meetings of the International Working Group are private and members are required to complete a WHO declaration of interest form before the meeting. Observers from the WHO Collaborating Centre for International Drug Monitoring, the WHO Collaborating Centre for Drug Utilization Research & Clinical Pharmacological Services and the International Federation of Pharmaceutical Manufacturers Association are also invited to attend the meetings of the International Working Group.

An open session is held prior to one of the semi-annual meetings to which any interested party can register (see further information below). Decision-making parts of meetings of the International Working Group will continue to be held in private. Decisions on ATC classification or DDD assignment are published on the website of the WHO Collaborating Centre for Drug Statistics Methodology and in the publication WHO Drug Information. Any decision on a new or revised ATC classification or DDD assignment is first published as temporary. Any interested party wishing to dispute this decision is invited to comment within a specified deadline after its publication. If there are no objections to a temporary decision, then it will be published as a final decision and implemented in the next issue of the ATC classification index with DDDs. If there is an objection then the decision will be reconsidered at the next meeting of the International Working Group. If a new decision is taken at the second meeting, the new decision will be published as temporary and will be open to comments similar to the first decision. WHO has the final responsibility for any decisions to be taken and any dispute arising in the course of this work must be referred to WHO for final resolution.

Open Session

The open session is held once a year in connection with the meeting of the WHO International Working Group for Drug Statistics Methodology. It is held in the interest of transparency and consists of one hour and a half prior to the closed decision-making session of the meeting.

It is open to anyone with a legitimate interest in the Anatomical Therapeutic Chemical (ATC) classification system and Defined Daily Dose (DDD) assignment. This includes regulatory authorities, the pharmaceutical industry, academia and non-governmental organisations.

It provides an opportunity for these persons to present additional information to the experts to assist them in their decision making.

It provides an opportunity for the international experts of the Working Group to exchange ideas and opinions with interested parties.

It is not intended to be used as a mechanism to challenge the decision of the Working Group. The procedures for applying for and commenting on an ATC classification or a DDD assignment are outlined in these *Guidelines* (see section V).

Interested parties are requested to register for this session to WHO Headquarter at least 14 days in advance of the meeting and are requested to provide a relevant reason for attending. WHO Headquarter will restrict the time allowed for each presentation in order to keep the duration of the open session within 1.5 hours. Information on these meetings will be made available on the WHO website at www.who.int/medicines.

C. The purpose of the ATC/DDD system

The purpose of the ATC/DDD system is to serve as a tool for drug utilization research in order to improve quality of drug use. One component of this is the presentation and comparison of drug consumption statistics at international and other levels.

A major aim of the Centre and Working Group is to maintain stable ATC codes and DDDs over time to allow trends in drug consumption to be studied without the complication of frequent changes to the system. There is a strong reluctance to make changes to classifications or DDDs where such changes are requested for reasons not directly related to drug consumption studies. For this reason the ATC/DDD system by itself is not suitable for guiding decisions about reimbursement, pricing and therapeutic substitution.

The classification of a substance in the ATC/DDD system is not a recommendation for use, nor does it imply any judgements about efficacy or relative efficacy of drugs and groups of drugs.

II. THE ANATOMICAL THERAPEUTIC CHEMICAL (ATC) CLASSIFICATION SYSTEM

A. Structure and nomenclature

Structure

In the Anatomical Therapeutic Chemical (ATC) classification system, the active substances are divided into different groups according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties.

Drugs are classified in groups at five different levels. The drugs are divided into fourteen main groups (1st level), with pharmacological/therapeutic subgroups (2nd level). The 3rd and 4th levels are chemical/pharmacological/therapeutic subgroups and the 5th level is the chemical substance. The 2nd, 3rd and 4th levels are often used to identify pharmacological subgroups when that is considered more appropriate than therapeutic or chemical subgroups.

The complete classification of metformin illustrates the structure of the code:

A	Alimentary tract and metabolism (1st level, anatomical main group)
A10	Drugs used in diabetes (2nd level, therapeutic subgroup)
A10B	Blood glucose lowering drugs, excl. insulins (3rd level, pharmacological subgroup)
A10BA	Biguanides (4th level, chemical subgroup)
A10BA02	metformin (5th level, chemical substance)

Thus, in the ATC system all plain metformin preparations are given the code A10BA02.

Nomenclature

- International nonproprietary names (INN) are preferred. If INN names are not assigned, USAN (United States Adopted Name) or BAN (British Approved Name) names are usually chosen.
- WHO's list of drug terms (Pharmacological action and therapeutic use of drugs - List of Terms) is used when naming the different ATC levels.

B. Inclusion and exclusion criteria

The WHO Collaborating Centre in Oslo establishes new entries in the ATC classification on *requests* from the users of the system. These include manufacturers, regulatory agencies and researchers. The coverage of the system is not comprehensive. A major reason why a substance is not included is that no request has been received.

Active ingredients which fulfil one of the following criteria will normally be included in the ATC system:

- they are new chemical entities (active ingredients) or biologicals proposed for licensing in a range of countries. A new chemical entity is normally not included in the ATC system before an application for marketing authorisation is submitted in at least one country.
- they are existing well defined chemical entities used in a variety of countries. An INN should preferably be established for the active ingredient. Alternatively other official names, e.g. USAN or BAN names should be available.
- they are herbal medicinal products assessed and approved by regulatory authorities based on dossiers including efficacy, safety, and quality data (e.g. the well-established use procedure in EU).

Other medicinal products are considered on a case by case basis. Complementary, homeopathic and herbal traditional medicinal products are in general not included in the ATC system.

C. Principles for classification

1. General Principles

Medicinal products are classified according to the main therapeutic use of the main active ingredient, on the basic principle of only one ATC code for each route of administration (i.e. pharmaceutical forms with similar ingredients and strength will have the same ATC code).

Immediate and slow release tablets will normally have the same ATC code.

A medicinal product can be given more than one ATC code if it is available in two or more strengths or routes of administration with clearly different therapeutic uses.

Two examples of this are as follows:

- Sex hormones in certain dosage forms or strengths are only used in the treatment of cancer and are thus classified under L02 - *Endocrine therapy*. Remaining dosage forms/strengths are classified under G03 - *Sex hormones and modulators of the genital system*.
- Clonidine is available in two different strengths. One strength, which is used mainly in the treatment of hypertension, is classified under C02 - *Antihypertensives*. Another strength mainly used in the treatment of migraine is classified under N02C - *Antimigraine preparations*.

Different pharmaceutical forms for topical and systemic use are also given separate ATC codes.

Example:

Prednisolone in single ingredient products is given several ATC codes due to different therapeutic use and different local application formulations.

A07EA01	Intestinal antiinflammatory agents	(enemas and foams)
C05AA04	Antihemorrhoidals for topical use	(suppositories)
D07AA03	Dermatological preparations	(creams, ointments and lotions)
H02AB06	Corticosteroids for systemic use	(tablets, injections)
R01AD02	Nasal decongestants	(nasal sprays/drops)
S01BA04	Ophthalmologicals	(eye drops)
S02BA03	Otologicals	(ear drops)

A medicinal product may be used for two or more equally important indications, and the main therapeutic use of a drug may differ from one country to another. This will often give several classification alternatives. Such drugs are usually only given one code, the main indication being decided on the basis of the available literature. Problems are discussed in the WHO International Working Group for Drug Statistics Methodology where the final classification is decided. Cross-references will be given in the guidelines to indicate the various uses of such drugs.

The ATC system is not strictly a therapeutic classification system. At all ATC levels, ATC codes can be assigned according to the pharmacology of the product. Subdivision on the mechanism of action will, however, often be rather broad, since a too detailed classification according to mode of action often will result in having one substance per subgroup which as far as possible is avoided (e.g. antidepressants). Some ATC groups are subdivided in both chemical and pharmacological groups (e.g. ATC group J05A - *Direct acting antivirals*).

If a new substance fits in both a chemical and pharmacological 4th level, the pharmacological group should normally be chosen.

Substances classified in the same ATC 4th level cannot be considered pharmacotherapeutically equivalent since their mode of action, therapeutic effect, drug interactions and adverse drug reaction profile may differ.

Normally, different stereoisomeric forms will have separate ATC codes. Exceptions will be described in the guidelines for the respective ATC groups.

A new medicinal substance not clearly belonging to any existing ATC 4th level group of related substances will as a main rule be placed in an X group ("other" group). To avoid a situation of several 4th levels with only one single substance in each, new 4th levels are as a general rule only established when at least two substances with marketing authorisations fit in the group. In addition, a new 4th level should be regarded a benefit for drug utilization research. New and innovative medicinal products will therefore often be classified in an X group and such groups could be established for only one single substance.

Prodrugs are usually assigned separate ATC codes if the dosages used are different and/or the nonproprietary name of the prodrug and the active drugs are different.

Example:

J01CA08 *pivmecillinam*
J01CA11 *mecillinam*

2. Classification of plain products

Plain products are defined as:

- Preparations containing one active component (including stereoisomeric mixtures).
- Medicinal products which in addition to one active component contain auxiliary substances intended to increase the stability of the preparations (e.g. vaccines containing small amounts of antibacterials), increase the duration (e.g. depot formulations) and/or increase the absorption (e.g. different solvents in various dermatologicals) are also considered as plain products.

Plain products are classified according to the general principles outlined in section II C1.

3. Classification of combination products

Products containing two or more active ingredients are regarded as combination products. Combination products are classified according to three main principles.

- a) Combination products containing two or more active ingredients belonging to the same 4th level are normally classified using the 5th level codes 20 or 30.

Example:

N01BB02 *lidocaine*
N01BB04 *prilocaine*
N01BB20 *combinations* (e.g. lidocaine and prilocaine)

- b) Combination products containing two or more active ingredients not belonging to the same 4th level are classified using the 50-series.

Example:

R06AA02 *diphenhydramine*
R06AA52 *diphenhydramine, combinations*

Different combination products sharing the same main active ingredient are usually given the same ATC code. Thus, products containing phenylpropanolamine + brompheniramine and phenylpropanolamine + cinnarizine are both given the code R01BA51.

Packages comprising two or more different medicinal products marketed under a common brand name are also considered as combination products.

E.g.: Sotalol tablets and aspirin tablets in one combination package is classified in C07AA57 *sotalol, combinations*.

- c) Combination products containing psycholeptic drugs, which are not classified under N05 - *Psycholeptics* or N06 - *Psychoanaleptics*, are classified at separate 5th levels using the 70-series.

Example:

N02BA71 - *acetylsalicylic acid, combinations with psycholeptics* (products containing other substances in addition to a psycholeptic are also classified here.)

Some of the combination products containing psycholeptics have been classified at a separate third or fourth level (e.g. A03C - *Antispasmodics in combination with psycholeptics*).

There are some exceptions to the main rules and these are explained in the guidelines.

Separate ATC 3rd or 4th levels have been assigned for some important combinations, e.g. beta blocking agents and diuretics.

It may be difficult to decide where a certain combination should be classified. The main therapeutic use decides the classification. A medicinal product containing an analgesic and a tranquillizer, and used primarily to ease pain, should be classified as an analgesic. Likewise, a preparation used for functional gastrointestinal disorders will be classified under A03, *Drugs for functional gastrointestinal disorders*, even if it contains small amounts of analgesics and/or psycholeptics. Similar examples are described in detail in the guidelines for the relevant drug groups.

In some ATC groups a ranking is introduced to help in the classification of combination products (e.g. combinations of different antihypertensives and combinations of different analgesics). This ranking shows which drug takes precedence over others when the classification is decided. This is detailed in the guidelines for the relevant drug groups.

D. Principles for changes to ATC classification

As the drugs available and their uses are continually changing and expanding, regular revisions of the ATC system will always be necessary.

Principle

Changes in the ATC classification should be kept to a minimum. Before alterations are made, difficulties arising for the users of the ATC system are considered and related to the benefits achieved by the alteration.

Alterations in ATC classification are made when the main use of a drug has clearly changed, and when new groups are required to accommodate new substances or to achieve better specificity in the groupings.

When it is decided to make an alteration, the following principles are used:

- Space is provided for possible future extension of an ATC group.
- The ATC code assigned to combination products should correspond as far as possible with the classification of the single substances in question.
- Previous ATC codes for deleted products are not used for new substances.
- Obsolete drugs or drugs withdrawn from the market are kept in the ATC system, since exclusion of substances from the ATC system may create difficulties for the users of the system when considering historical data.
- Changes of currently valid codes are kept to a minimum. A gap in the sequence is preferred to changing codes.

When an ATC code is altered, the DDD is also reviewed. For example, when the classification of chloroquine was changed from ATC group M to P (i.e. classified only as an antimalarial), the DDD was changed since the dosages used for treatment of malaria are different from the dosages used for rheumatic disorders.

E. The EphMRA classification system

The ATC classification system was originally based on the same main principles as the Anatomical Classification (AC-system) developed by the European Pharmaceutical Market Research Association (EphMRA) and the Pharmaceutical Business Intelligence and Research Group (PBIRG). In the EphMRA system, drugs are classified in groups at three or four different levels. The ATC classification system is modified and extended from the EphMRA system by the addition of a therapeutic/pharmacological/chemical subgroup as the fourth level and a fifth level for the chemical substance.

Since 1991 there has been a consultation between the EphMRA classification committee and the WHO Collaborating Centre for Drug Statistics Methodology in order to achieve a better harmonisation between the two systems. The aim of this harmonisation process is to make the systems consistent down to the ATC 3rd level, where this is possible, and to describe the differences (i.e. show the differences by giving bridges) and similarities in groups where harmonisation is not

achieved. The harmonisation process was initiated in order to minimise the confusion of having two very similar classification systems.

It should be emphasised that there are many differences between the EphMRA classification and the ATC classification. This means that data prepared using the ATC classification cannot be directly compared with data prepared using the EphMRA system. The abbreviation ATC is unfortunately also used for the EphMRA classification, which can cause confusion.

The EphMRA classification system is used worldwide by IMS (Intercontinental Medical Statistics) in producing marketing research statistics for the pharmaceutical industry.

III. DDD (DEFINED DAILY DOSE)

A. Definition and general considerations

The basic **definition** of the unit is:

The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults.

A DDD will only be assigned for drugs that already have an ATC code.

It should be emphasised that the defined daily dose is a unit of measurement and does not necessarily reflect the recommended or Prescribed Daily Dose (see page 31). Doses for individual patients and patient groups will often differ from the DDD and will necessarily have to be based on individual characteristics (e.g. age and weight) and pharmacokinetic considerations.

For the optimal use of drugs, it is important to recognise that genetic polymorphism due to ethnic differences can result in variations in pharmacokinetics of drugs. However, only one single DDD is assigned per ATC code and route of administration. The DDD should reflect global dosage irrespective of genetic variations.

Drug consumption data presented in DDDs only give a rough estimate of consumption and not an exact picture of actual use. DDDs provide a fixed unit of measurement independent of price, currencies, package size and strength enabling the researcher to assess trends in drug consumption and to perform comparisons between population groups.

DDDs are not established for topical products, sera, vaccines, antineoplastic agents, allergen extracts, general and local anesthetics and contrast media.

B. Principles for DDD assignment

The basic principle is to assign only one DDD per route of administration within an ATC code.

DDDs for plain substances are normally based on monotherapy. Exceptions to this rule are given in the guidelines.

A DDD will normally not be assigned for a substance before a product is approved and marketed in at least one country.

For substances indicated for rare disorders with individual dosing, the Working Group could decide not to assign a DDD.

1. Plain products

Plain products contain one active ingredient (including stereoisomeric mixtures). See page 18.

When a new DDD is assigned, various sources are used to get the best overview of the actual or expected use of a substance. The assigned DDD is based on the following principles:

- The average adult dose used for the main indication as reflected by the ATC code. When the recommended dose refers to body weight, an adult is considered to be a person of 70 kg. It should be emphasised that even special pharmaceutical forms mainly intended for children (e.g. mixtures, suppositories) are assigned the DDD used for adults. Exceptions are made for some products only used by children, e.g. growth hormones and fluoride tablets.
- The maintenance dose (long term therapeutic dose) is usually preferred when establishing the DDD. The initial dose may differ but this is not reflected in the DDD. If the approved dose recommendation provides limited information about maintenance dose, the DDD will usually be the average of the maintenance dose range. Examples of interpretation of approved dose titration recommendations:
 - “Titrate up to a high dose if it is tolerated”: the high dose would normally be chosen as the DDD.
 - “Consider to increase the dose only if efficacy is not satisfactory with initial dose”: the DDD would normally be based on the initial dose.

- For some groups of medicinal products specific principles for DDD assignment are established (e.g. the DDDs for the selective serotonin agonists in the treatment of migraine are based on the approved initial dose). These principles are given in the guidelines.
- The treatment dose is generally used. If, however, prophylaxis is the main indication, this dose is used, e.g. for fluoride tablets (A01AA01) and some antimalarials.
- A DDD is usually established according to the declared content (strength) of the product. Various salts of a substance are usually not given different DDDs. Exceptions are described in the guidelines for the different ATC groups. For example, the DDDs for antimalarials are expressed as the base.
- Normally, different stereoisomeric forms are assigned separate DDDs and ATC codes. The DDDs for stereoisomeric forms are described in the respective ATC groups.
- Prodrugs, which have not been given a separate ATC code, are normally not given a separate DDD.
- The DDD is often identical for various dosage forms of the same drug. Different DDDs may be established when the bioavailability is substantially different for various routes of administration (e.g. oral and parenteral administration of morphine) or if the dosage forms are used for different indications. When the use of parenteral formulations represents only a minor fraction of the total use for a specific indication, these products do not receive a separate DDD even if the bioavailability of the oral form is substantially different.
- Parenteral products intended for i.v. and i.m. administration have the same DDD.

*The DDD is nearly always a **compromise** based on a review of the available information including doses used in various countries when this information is available. The DDD is sometimes a dose that is rarely if ever prescribed, because it is an average of two or more commonly used dose sizes.*

2. Combination products

The DDDs assigned for combination products are based on the main principle of counting the combination as one daily dose, regardless of the number of active ingredients included in the combination. If a treatment schedule for a patient includes e.g. two single ingredient products, then the consumption will be measured by counting the DDDs of each single ingredient product separately. If, however, a treatment schedule includes a combination product containing two active ingredients, then the calculated consumption measured in DDDs will normally be lower since the DDD for the combination will be counted.

Example I:

Treatment with two products, each containing one active ingredient:

Product A: Tablets containing 20 mg of substance X (DDD = 20 mg)

Product B: Tablets containing 25 mg of substance Y (DDD = 25 mg)

The dosing schedule 1 tablet of A plus 1 tablet of B daily will be calculated as a consumption of 2 DDDs.

Example II:

Treatment with a combination product containing two active ingredients:

Product C: Tablets containing 20 mg of substance X and 12.5 mg of substance Y.

The DDD of the combination products is assigned as 1 UD = 1 tablet.

The dosing schedule 1 tablet of C daily will be calculated as 1 DDD (even though it will be equivalent to 1.5 DDD of the single active ingredients).

The following principles for assigning DDDs to combination products apply:

1. For combination products (other than the combination products used in hypertension, see point 2 below) where the ATC code identifies the main ingredient (i.e. for the 50- and 70-series combinations and for some 4th level combinations), the DDD for the combination product should be equal to the DDD for the main active ingredient.
2. For combination products used for treatment of hypertension (i.e. ATC group C02L, C02N, C03E, C07B-F, C08 and C09), DDDs are based on the average number of dosing intervals per day. This means that: 1 tablet is the DDD for combinations given once daily, whereas 2 tablets is the DDD for combinations given twice daily and 3 tablets is the DDD for combinations given three times daily etc. This principle means that the assigned DDDs may differ from the DDD assigned for the main active ingredient (according to ATC code).

For all combination products where the DDD assigned deviates from the principles given above, a list of DDDs are available from the Centre (published on the website www.whooc.no).

3. Other factors

a) Fixed dose groups

For some groups of products, it has been considered most appropriate to estimate the average use for products within a group instead of establishing accurate doses for every product, e.g. cough mixtures in ATC group R05 and multivitamins in ATC group A11. For the multivitamins the composition of various products may differ, but the average recommended dose is usually the same. Such DDDs are called "fixed dose".

In some ATC groups, it has been decided to use fixed DDDs for all combination products given in e.g. number of tablets regardless of strength. These rules are clearly stated in the chapters in the respective ATC levels in this publication (e.g. ATC group A02AD, A02BD and A02BX).

For eye drops used in glaucoma therapy, a fixed dose regardless of strength has been established in the different subgroups. This is based on the assumption that, per dosage given, only one drop is applied in each eye, regardless of strength.

When fixed doses are assigned, these will be further described in the guidelines for the different ATC groups.

b) Depot formulations

Depot formulations (e.g. sustained release formulations) are usually assigned the same DDDs as the ordinary dosage forms. Exceptions to this main rule are described in the guidelines for the different ATC groups.

c) Intermittent dosing

In certain therapeutic groups, e.g. hormones, many of the products are administered intermittently. In such cases, the dose administered is divided by the number of days in the treatment period to obtain the average daily dose. This means that medicament free periods in between courses are included in the treatment period. This also applies to such drugs as depot antipsychotics and contraceptive pills, which are given intermittently.

d) Duration of treatment

The duration of treatment is normally not considered when assigning a DDD, even if the drugs are used mainly in short periods. Exceptions from this main rule are explained in the respective ATC groups.

4. Selection of units

For plain products, DDDs are as far as possible given in amount of active ingredients, using the following units: g (gram), mg (milligram), mcg (microgram), mmol (millimol), U (unit), TU (thousand units) and MU (million units). The abbreviation U for unit is used for international as well as other units.

For combination products or products where a DDD for various reasons cannot be given in amount of active ingredient, the unit UD (unit dose) is used:

- Tablets, suppositories, pessaries, etc:
1 UD equals 1 tablet, 1 suppository, 1 pessary etc.
- Powder for oral use:
1 UD equals 1 gram of powder. If the DDD for an oral powder is given in grams, this refers to the content of active ingredient.
- Powder in single dose units for oral use:
1 UD equals 1 unit dose powder.
- Powder for injection:
1 UD equals 1 gram of powder. If the DDD for powder for injection is given in grams, this refers to the content of active ingredient.
- Powder for inhalation:
1 UD equals 1 unit dose powder, e.g. 1 capsule.
- Liquid preparations for oral use (mixtures, syrups etc.):
1 UD equals 5 ml of the preparation.
- Liquid preparations for parenteral use (injections):
1 UD equals 1 ml of the preparation.
- Liquid preparations for rectal use:
1 UD equals 1 ml of the preparation.

- Liquid preparations for inhalation:
1 UD equals 1 ml of the preparation.
- Liquid preparations for inhalation in single dose units (unit dose):
1 UD equals 1 unit dose inhal.sol
- Enemas:
1 UD equals 1 enema.
- Plaster for transdermal application:
1 UD equals 1 plaster.
- Vaginal cream:
1 UD equals 1 dose, 1 application.

Route of administration

The route of administration is indicated by the following codes:

Inhal	= Inhalation	R	= Rectal
N	= Nasal	SL	= Sublingual/buccal
O	= Oral	TD	= Transdermal
P	= Parenteral	V	= Vaginal

C. Pediatric DDD

DDDs are normally assigned based on use in adults (see page 22).

For medicinal products approved for use in children, the dose recommendations will differ based on age and body weight. Many medicinal products used on children are not even approved for such use, and documentation regarding dose regimens is not available.

Thus the WHO International Working Group for Drug Statistics Methodology has concluded that pediatric DDDs are impossible to assign and problems related to drug utilization research in children cannot be solved by such means.

Estimating prevalence of drug use in children is not possible by using crude sales data presented in DDDs. Prescribed daily dosages and indications in a pediatric population should be used if available and compared with the DDD values. If the pediatric subgroup is difficult to identify, the general DDD should be used as a measuring tool for overall comparisons.

D. Principles for reviewing and changing DDD

As the dosages used may change over time, it will always be necessary to make some alterations. The International Working Group for Drug Statistics Methodology may review a DDD whenever the Group finds it appropriate.

Changes of DDDs should be kept to a minimum and avoided as far as possible. Too many alterations will always be disadvantageous for long-term studies on drug utilization. Before alterations are made, difficulties arising for the users are weighed against the benefits achieved by the alteration.

- The same principles used to assign new DDDs also apply when DDDs are reviewed.
- Changes are generally not made unless they are at least in the order of 50 %. This rule is not used for the three year revision of DDDs, where smaller alterations are allowed. Further, minor alterations are allowed for important drugs, which are frequently used (e.g. the DDD for cimetidine was changed from 1.0 g to 0.8 g).

DDD review after three years

All newly assigned DDDs are reviewed during the third year after inclusion in the *ATC Index with DDDs*. The DDDs are reviewed at the first semi-annual meeting of the International Working Group for Drug Statistics Methodology. The following are considered:

- Recommended dosages as listed in drug catalogues in different countries and/or published in peer reviewed scientific journals or major international textbooks.
- Data on prescribed daily doses (PDDs) from a range of countries. Figures showing the prescribed daily dose (PDD) are important when reviewing an assigned DDD. Usually more data concerning PDDs are available after a three years period than at the time of marketing.
- Established main indication and therapy profile of the preparation (i.e. has the main indication changed?)
- Existing DDDs in the ATC group.
- Written objections to the DDD which have been received.

When reviewing combination products, changes in the DDDs for the different active ingredients are an important consideration.

Further reviews of DDDs

After the first three years period, the DDD normally remains unchanged for at least five years unless the WHO Working Group decides to make a total revision of all DDDs assigned in an ATC group. Proposed DDD changes from users of the system, based on **new** information will always be considered, but only after the three years revision has been performed.

E. Description of other drug utilization metrics

Cost

Drug use can be expressed in terms of costs (e.g. national currency). Cost figures are suitable for an overall cost analysis of drug expenditure. National and international comparisons based on cost parameters are often misleading and of limited value in the evaluation of drug use. Price differences between alternative preparations and different national cost levels make the evaluation difficult. Long-term studies are also difficult due to fluctuations in currency and changes in prices.

When cost data are used, an increase in the use of cheaper drugs may have little influence on the total level, while a shift to more expensive drugs is more readily noticed.

Volume

Common physical units (e.g. grams, kilos, litres), numbers of packages or tablets and numbers of prescriptions are also used for quantifying drug consumption. These units can be applied only when the use of one drug or of well defined products is evaluated. Problems arise, however, when the consumption of whole drug groups is considered.

If consumption is given in terms of grams of active ingredients, drugs with low potency will have a larger fraction of the total than drugs with high potency. Combined products may also contain different amounts of active ingredients from plain products, which will not be reflected in the figures.

Counting numbers of tablets also has disadvantages, because strengths of tablets vary, with the result that low strength preparations contribute relatively more than high strength preparations. Also, short-acting preparations will often contribute more than long-acting preparations.

Numbers of prescriptions do not give a good expression of total use, unless total amounts of drugs per prescription are also considered. Counting of prescriptions, however, is of great value in measuring the frequency of prescriptions and in evaluating the clinical use of drugs (e.g. diagnosis and dosages used).

Prescribed daily dose

The prescribed daily dose (PDD) can be determined from prescription studies, medical- or pharmacy records and patient interviews. It is important to relate the PDD to the diagnosis on which the dosage is based. The PDD will give the average daily amount of a drug that is actually prescribed. When there is a substantial discrepancy between the PDD and the defined daily dose (DDD), it is important to take this into consideration when evaluating and interpreting drug consumption figures.

For drugs where the recommended dosage differs from one indication to another (e.g. the antipsychotics) it is important that diagnosis is linked to the prescribed daily dose given. Pharmacoepidemiological information (e.g. sex, age and mono/combined therapy) is also important in order to interpret a PDD. The PDD can vary according to both the illness treated and national therapy traditions. For the anti-infectives, for instance, PDDs vary according to the severity of the infection. There are also substantial differences between PDDs in various countries, which can be up to a four to five fold range. PDDs in Asian populations are often lower than in Caucasian populations. The fact that PDDs may differ from one country to another should always be considered when making international comparisons.

It should be noted that the prescribed daily dose does not necessarily reflect actual dose consumed.

IV. USE AND MISUSE OF THE ATC/DDD SYSTEM

The main purpose of the ATC/DDD system is as a tool for presenting drug utilization statistics with the aim of improving drug use. This is the purpose for which the system was developed and it is with this purpose in mind that all decisions about ATC/DDD classification are made. Consequently, using the system for other purposes can be inappropriate. The system has been used since the early 1970s in drug utilization studies where it has been demonstrated to be suitable for national and international comparisons of drug utilization, for the evaluation of long term trends in drug use, for assessing the impact of certain events on drug use and for providing denominator data in investigations of drug safety (see also point I C The purpose of the ATC/DDD system, page 14).

National implementation of the ATC/DDD methodology

For monitoring and comparing drug use internationally it is important to ensure that the data retrieved are comparable. In order to facilitate data collection it is recommended to establish national medicinal product registries. It is recommended to have a common structure of these registries. The ATC code and DDD should be

linked to each medicinal product on the package level. National registries should as a minimum include the following variables:

- Unique identifier (registration number)
- Medicinal product name (brand name/trademark)
- Pharmaceutical form
- Strength
- Pack size
- ATC code
- Active ingredient(s)
- DDD
- Route of administration
- Number of DDDs in the pack

For an extended list of recommended variables to be included in a national medicinal product registry, see EURO-MED-STAT (<http://www.euromedstat.cnr.it/>).

It is of vital importance that the ATC code is correctly linked to each medicinal product package. The number of DDDs per package should be calculated for each medicinal product package.

Good procedures for updating national registries with new ATC codes/DDDs and alterations should be established. It is recommended that the responsibility for quality assurance and validation of national registries is allocated to a national body in each country. This work should be performed by competent persons with good knowledge of the ATC/DDD methodology.

An updated version of the *ATC/DDD Index* is issued in January each year. To be able to compare drug utilization data from different countries and time periods, it is essential to know which ATC codes and DDDs are used. A minimum number of changes in the ATC codes and DDDs are made annually. Thus, it is important to give proper references to the ATC/DDD version used when presenting drug consumption figures.

A publication entitled "*Introduction to Drug Utilization Research*" is available from WHO Geneva.

A. Drug utilization

The ATC/DDD system can be used for collection of drug utilization statistics in a variety of settings and from a variety of sources.

Examples are:

- Sales data such as wholesale data at a national, regional or local level.
- Dispensing data either comprehensive or sampled. Computerised pharmacies can easily collect data on drugs dispensed. Alternatively, sample data can be collected manually. Reimbursement systems, which operate in a number of countries at the national level provide comprehensive dispensing data down to the individual prescription level, as all prescriptions are submitted and recorded for reimbursement. This is generally called “claims” data. Similar data are often available through health insurance or health maintenance organisations.

These databases can sometimes allow collection of demographic information on the patients, and information on dose, duration of treatment and co-prescribing. Less commonly, linkage to hospital and medical databases can provide information on indications, and outcomes such as hospitalisation, use of specific medical services, and adverse drug reactions.

- Patient encounter based data. This is usually collected by specially designed sampling studies such as those carried out by market research organisations. However, increasing use of information technology at the medical practice level will make such data available more widely in the near future. These methods have the advantage of potentially providing accurate information on Prescribed Daily Doses, patient demographics, duration of therapy, co-prescribing, indications, morbidity and co-morbidity, and sometimes outcomes.
- Patient survey data. Collection of data at the patient level can provide information about actual drug consumption and takes into account compliance in filling prescriptions and taking medications as prescribed. It can also provide qualitative information about perceptions, beliefs, and attitudes to the use of medicines.
- Health Facility data. Data on medication use at all the above levels is often available in health care settings such as hospitals and health centres at regional, district, or village level.

Use of the ATC/DDD system allows standardisation of drug groupings and a stable drug utilization metric to enable comparisons of drug use between countries, regions, and other health care settings, and to examine trends in drug use over time and in different settings.

Drug consumption figures should preferably be presented as numbers of DDDs/1000 inhabitants/day or, when in-hospital drug use is considered, as DDDs per 100 bed days. Sales or prescription data presented in DDD/1000 inhabitants/day may provide a rough estimate of the proportion of the population within a defined area treated daily with certain drugs. For example, the figure 10 DDDs/1000 inhabitants/day indicates that 1% of the population on average gets a certain treatment daily.

For antiinfectives (or other drugs normally used in short periods) it is often considered most appropriate to present the figures as numbers of DDDs per inhabitant per year, which will give an estimate of the number of days for which each inhabitant is, on average, treated annually. For example, 5 DDDs/inhabitant/year indicates that the consumption is equivalent to the treatment of every inhabitant with a 5 days course during a certain year.

Alternatively, if the standard treatment period is known, the total number of DDDs can be calculated as the number of treatment courses, and the number of treatment courses can then be related to the total population.

For some drug groups where DDDs have not been established, alternative ways of presenting data are recommended. For example, consumption of dermatological preparations can be presented in grams of ointment, cream etc, and antineoplastic agents ATC group L01 can be presented in grams of active ingredient.

When there is a known discrepancy between the prescribed daily dose (PDD) and the DDD, it is important to take this into account when interpreting drug consumption figures. Caution should also be taken in situations where the recommended dosage differs from one indication to another (e.g. antipsychotics), in severe versus mild disease (e.g. antibiotics) and where PDDs may differ from one population to another (e.g., according to sex, age, ethnicity or geographic location).

Finally, it should be taken into considerations that some prescribed medications are not dispensed, and the patient does not always take all the medications, which are dispensed. Specially designed studies are required to measure actual drug intake at the patient level.

Since alterations of ATC and DDDs do occur it is important to be aware of which version of the ATC index is used in drug consumption studies especially when comparing the data over time and when making international comparisons.

It is recommended that data are updated (recalculated) by using the most recent version of the ATC Index.

B. Improving drug use

Collecting and publishing drug utilization statistics are critical elements in the process of improving the prescription and dispensing of medicines. For drug utilization statistics to have the best possible impact on drug use, the statistics need to be used in a focused and active manner.

Examples of ways in which drug utilization statistics based on ATC and DDDs have been and can be used to improve drug use include the following:

- National publications, which provide clinicians, pharmacists and others with a profile of drug consumption in the country (with or without comparisons between countries or between areas within the country).
- Publications providing feedback within health services to individual health facilities, groups of health care providers, or individual health providers.
- Use of drug utilization statistics by national health systems, universities, drug information centres, and others to identify possible over use, underuse or misuse of individual drugs or therapeutic groups. Depending on the situation this information can then be used to initiate specific studies or specific educational interventions. Educational interventions may include articles in drug bulletins, articles in scientific journals, letters to clinicians, etc.

C. Drug Safety Assessment

Estimates of frequency trends in spontaneously reported cases of suspected adverse reactions for certain population groups may be linked to trends in drug consumption, using the ATC/DDD system. Use of the DDD/1000 inhabitants/day as a drug utilization metric as the denominator, where frequency of adverse reactions is the numerator, allows trends in the frequency of adverse reaction reports to be examined against trends in drug utilization. For comparisons between drugs, validation by PDDs would be necessary.

The WHO Collaborating Centre for International Drug Monitoring (Uppsala Monitoring Centre), Sweden, receives spontaneous reports of suspected adverse reactions from national centres (96 countries are included in the programme, October 2009). Information on all medicinal products appearing in these reports is stored in a drug register, linked to the reports database. All single and multiple ingredient preparations are given an ATC code at the substance level, which allows flexible searches comprising different drug categories or groups of drugs. The ATC system is also used for the grouping of drugs in output documents.

D. "Double medication" and "pseudo-double medication"

The ATC classification can be used as a tool for screening of "double"- and "pseudo-double medication".

"Double medication" can be defined as using two identical drugs simultaneously (e.g. two different diazepam preparations) whereas "pseudo-double medication" can be defined as using two chemically different substances but with similar pharmacodynamic properties simultaneously (e.g. a diazepam preparation plus an oxazepam preparation).

The objective of checking these situations, by using physician or pharmacy patient computer records, is to prevent unnecessary medication, which may increase the risk of side effects.

In the case of plain preparations, the ATC 5th level codes can be used; while the level to which monitoring must be made depends on the ATC group concerned. For combination products the ATC 5th level code is not always sufficient to identify all active ingredients. It is therefore recommended to connect all ATC codes given for each of the different active ingredients to each combined preparation.

E. Drug catalogues

ATC codes are included in some international drug catalogues (e.g. the Martindale) and in several national drug catalogues.

F. Drug costs, pricing and reimbursement and cost-containment

Basing detailed reimbursement, therapeutic group reference pricing and other specific pricing decisions on the ATC and DDD assignments is a misuse of the system. This is because the ATC and DDD assignments are designed solely to maintain a stable system of drug consumption measurement, which can be used to follow and compare trends in the utilization of drugs within and across therapeutic groups. None the less, drug utilization data have a central role in the quality of care cycle and ATC and DDD methodologies can be helpful in following and comparing trends in cost, but need to be used with caution.

The DDD is a technical drug use metric. DDDs do not necessarily reflect therapeutically equivalent doses of different drugs and therefore cannot be assumed to represent daily doses that produce similar treatment outcomes for all products within an ATC category. Such estimates of therapeutic equivalence are very difficult to establish, particularly to the precision usually required for pricing decisions. DDDs, if used with caution can be used to compare, for example, the costs of two formulations of the same drug. However, it is usually not valid to use this metric to compare costs of different drugs or drug groups. The relationships between therapeutically equivalent doses, the actual prescribed daily dose (PDD) and DDD usually differ between drugs and, for the same drug, between countries. Moreover, even though PDDs commonly change over time altering a DDD complicates drug utilization research, hence there is a reluctance to alter a DDD. Alterations are not made unless there is evidence that changes in PDD are large, or there is some particular reason such as a change in the main indication. For these reasons, DDDs are not suitable for comparing drugs for specific, detailed pricing, reimbursement and cost-containment decisions.

Similarly, basing reimbursement and pricing comparisons on inclusion of drugs in ATC groups is not recommended. The main indications for drugs (on which ATC assignments are based) often differ widely between countries and, like the PDD, can change over time. However, the ATC classifications can be useful when costs need to be aggregated into drug groups or therapeutic areas to determine, for example, to what extent increased costs can be attributed to increased use of a therapeutic group over time.

G. Pharmaceutical marketing purposes

It is important to emphasise that the ATC classification does not necessarily reflect the recommended therapeutic use in all respects. Therefore, the ATC system should not be used as a tool for marketing purposes concerning efficacy, mechanism of action or therapeutic profile in relation to other drugs.

It should be emphasised that assignment to different ATC groups does not mean a difference in therapeutic effectiveness and assignment to the same ATC group does not indicate therapeutic equivalence.

Concerning use of price comparisons for marketing purposes, see point F above.

V. PROCEDURES AND DATA REQUIREMENTS FOR ATC/DDD ASSIGNMENT AND ALTERATIONS

A. Requests for ATC classification

1. Procedures and timing

All new entries in the ATC classification system are assigned on request from the users. Requests for ATC classification of a medicinal substance should be addressed to the WHO Collaborating Centre for Drug Statistics Methodology in Oslo, Norway. The application form for assignment of new ATC codes is shown in Annex I and is also available on our website www.whocc.no. Application for ATC/DDD is free of charge. The official language of the Centre is English. Requests and documentation should accordingly be submitted in English. If a substance marketed in a country is not included in the latest version of the annually updated ATC classification index, a request for an ATC code may in principle be sent from any user of the system (e.g. health authorities, pharmaceutical manufacturers, researchers and other users). It will usually be the manufacturer who has best access to the information required for an application. The manufacturer will usually wish to know about and be involved in an application for an ATC classification and/or DDD assignment for one of their products, particularly if it is a new drug. Other users of the system are therefore encouraged to work through the manufacturer in submitting applications. A national centre responsible for assigning ATC codes to national products marketed in the respective country, should preferably be established in each country.

A new chemical entity is normally not included in the ATC system before an application for marketing authorisations is submitted in at least one country. In some cases, it may be necessary to await a classification until the new medicinal product has been approved in at least one country (especially for chemical entities where it is considered difficult to establish a new 5th level). These conditions are set to avoid including in the ATC system too many chemical entities which never reach the market.

It is left to the national users of the ATC system to classify combination products based on the principles given in these guidelines. The guidelines are prepared in order to facilitate this work and to ensure that different users of the ATC system classify in a consistent way. If the content of these guidelines is not sufficient to decide a classification of a specific combination, or if it is necessary to establish a new ATC entry, such problems should be addressed to the WHO Centre in Oslo. The Centre also runs regular training courses to assist those working on the system at a national level.

The WHO International Working Group for Drug Statistics Methodology formally approves all new ATC codes. The group has two annual meetings, normally in March and October.

The steps in the approval procedure for new ATC codes are normally as follows:

- A standard letter confirming receipt of the request is returned from the Centre to the applicant.
- If the new code is easy to assign, a preliminary ATC code assigned by the Centre is returned to the applicant within 6-8 weeks, informing them that the ATC code still has to be formally approved by the Working Group at the next meeting.
- For substances with more than one alternative classification and for substances, which are difficult to classify into existing classifications, the requests are discussed in the Working Group before assignment of a temporary ATC code. The applicant receives this information within 6-8 weeks after receipt of the request. After approval of the minutes of the Working Group meetings, the decision concerning the respective ATC code is sent from the Centre to the applicant.
- After approval of the minutes of the Working Group meeting the new ATC codes approved at the meeting are published on the website www.whocc.no and in the next issue of the publication *WHO Drug Information*. A deadline will then be allowed for interested parties to comment or object to the decisions.
- If objections, justified on evidence submitted, are received, the ATC classification will be discussed again at the following meeting of the Working Group. If the decision is kept, then the decision is considered final after this meeting. If a new decision is taken by the Working Group, notification of this new ATC is published at our website www.whocc.no and in the next issue of the publication *WHO Drug Information*. A deadline is then allowed for any interested part to comment or object to the decision.

- If no objections are received, the new ATC code is considered final and included in the next issue of the ATC classification index. A list of new final ATC codes is also published semi-annually on the website www.whocc.no and in the *WHO Drug Information*.

In order to include requests for new ATC codes on the agenda for the Working Group meetings, they should normally be forwarded to the Centre before 15 January (March meeting) and before 15 August (October meeting). These dates should be considered as a guideline since there might be changes in the meeting dates from one year to another.

ATC codes approved at the March meeting (e.g. March 2011) will be included in the ATC index the following year (i.e. January 2012).

For ATC codes approved at the October meeting of the Working Group (e.g. October 2011), the new codes will appear in the ATC index the year after the following year (i.e. January 2013).

2. Data requirements for submission

The following data should be submitted when requesting an ATC code for a substance:

- Chemical structure and relationship to similar drugs
- Pharmacology and mechanism of action including receptor binding profiles and relationships to similar drugs
- Main indication as shown in the product information in major countries where it is licensed or submitted for licensing
- Other indications which are licensed or for which licensing is proposed in the future
- Proposed ATC classification with justification based on the evidence submitted
- Status concerning marketing authorisation
- Information about therapeutic use, if available

Useful sources of these data would be approved product information documents from major regulatory countries, or proposed product information documents stating that these are not yet approved. Summaries of submissions to, or evaluations from, major regulatory agencies relating to the above are useful, as well as market research data showing the percentage use for the main indications.

B. Requests for changes to ATC classifications

1. Procedures and timing

A change in the ATC classification should be proposed and explained in writing and addressed to the WHO Collaborating Centre for Drug Statistics Methodology. Any user may in principle propose changes to ATC classifications. There is no application form for ATC alterations. All proposals for changes will be discussed in the WHO International Working Group for Drug Statistics Methodology.

The steps in the evaluation procedure for changes to ATC classifications are as follows:

- The Centre will confirm receipt of the proposal for a change and give information about the time schedule for discussion at the Working Group meeting.
- After approval of the minutes of the Working Group meeting, the decision from the meeting concerning the proposed change is distributed from the Centre to those requesting the change (the applicant). Independent of whether it has been decided to change or not to change, a deadline will be allowed for the applicant to comment or object to this decision.
- If it is decided to make a change, notification of this change is published at our website www.whocc.no and in the next issue of the *WHO Drug Information*. A deadline is then allowed for any interested part to comment or object to the change.
- If objections, justified on submitted evidence, are received, the ATC alteration will be discussed again at the following meeting of the Working Group, and a final decision will then be taken.
- If no objections are received, the altered ATC classification will be implemented in the next issue of the ATC classification index.

In order to include proposals for ATC alterations on the agenda for the Working Group meetings, they should be forwarded to the Centre before 15 January (March meeting) and before 15 August (October meeting). These dates should be considered as a guideline since there might be changes in the meeting dates from one year to another.

ATC alterations decided at the March meeting (e.g. March 2011) will be included in the ATC index the following year (i.e. January 2012). ATC alterations decided at the October meeting of the Working Group (e.g. October 2011) will be included in the ATC index the year after the following year (i.e. January 2013).

2. Data requirements for submission

When requesting changes to ATC classifications, the data requirements are similar to the data required for new ATC codes. An important basis for the ATC/DDD system is to maintain a stable database for drug consumption studies. For this reason, there need to be compelling reasons for changing ATC codes. It is therefore important to submit data, which justify the proposed change.

If a change in the main therapeutic use is the reason for the proposed change, the data submitted should clearly indicate this change (e.g. market research data showing the percentage use for the different indications in a range of countries).

If new knowledge of pharmacology or mechanism of action is the reason for the proposed change, relevant evidence should be submitted.

If the proposed change is to establish specific ATC groups for one or more substances already classified in another group (usually a *various* group), it is necessary to submit data that verify that the change is beneficial and represents an improvement of the ATC classification for presenting drug consumption statistics. Justifications based on reimbursement, pricing or marketing reasons will not be considered.

C. Requests for DDD assignment

1. Procedures and timing

All new DDDs are assigned on request from the users. Requests for new DDDs should be addressed to the WHO Collaborating Centre for Drug Statistics Methodology. The application form for assignment of new DDDs is shown in Annex I and copies are available from the Centre (www.whocc.no). Any user may in principle propose a new DDD (e.g. health authorities, pharmaceutical

manufacturers, researchers and others). However, as with ATC code assignment, it is the manufacturer who will usually have the best access to the required information.

A DDD will only be assigned for substances which have received an ATC code, or where the ATC code can be assigned simultaneously with the DDD. DDDs are not assigned before marketing is approved in at least one country.

All new DDDs are discussed and approved by the WHO International Working Group for Drug Statistics Methodology.

The steps in the approval procedure for new DDDs are very similar to the procedure for new ATC codes (see page 38, 39):

- The Centre will confirm receipt of the request for a new DDD and give information to those requesting the DDD (the applicant) about the time schedule for discussion at the following Working Group meeting.
- After approval of the minutes of the Working Group meeting, the decision from the meeting concerning the DDD is distributed from the Centre to the applicant.
- The new DDDs are published on the website www.whocc.no and in the next issue of the WHO publication: *WHO Drug Information*. A deadline is then allowed for interested parties to comment or object to the new DDD.
- If objections, justified on submitted evidence, are received, the DDD will be discussed again at the following meeting of the Working Group. If the decision is kept, then the decision is considered final after this meeting. If a new decision is taken by the Working Group, notification of this new DDD is published at our website www.whocc.no and in the next issue of the publication *WHO Drug Information*. A deadline is then allowed for any interested part to comment or object to the decision.
- If no objections are received, the new DDD is considered final after the deadline, and included in the next issue of the ATC classification index (see page 42). A list of final DDDs is also published semi-annually at our website www.whocc.no and in the *WHO Drug Information*.

In order to include requests for new DDDs on the agenda for the Working Group meetings, they should be forwarded to the Centre before 15 January (March meeting) and before 15 August (October meeting). These dates should be

considered as a guideline since there might be changes in the meeting dates from one year to another.

New DDDs decided at the March meeting (e.g. March 2011) will be included in the ATC index the following year (i.e. January 2012). New DDDs decided at the October meeting of the Working Group (e.g. October 2011) will be included in the ATC index the year after the following year (i.e. January 2013).

2. Data requirements for submission

The following information is required when requesting a new DDD:

- Dose ranges and dosing instructions for each indication in the product information approved by one or more major regulatory authorities.
- Doses used in clinical trials to support marketing.
- Market research data on doses used in practice in a range of countries (developed and developing where available). The average used dose should be defined.
- Where the drug is to fit into an existing ATC classification, comparative dosing information should be provided where it is available. It is difficult to define therapeutically equivalent doses with the degree of precision often asked for, and the DDDs within therapeutic groups do not necessarily represent therapeutically equivalent doses.
- Proposal for a DDD justified by the submitted data.
- Status concerning marketing authorisation.

D. Requests for changes to DDDs

1. Procedures and timing

A change in DDDs should be proposed and explained in writing, and addressed to the WHO Collaborating Centre for Drug Statistics Methodology. Any user may in principle propose changes in DDDs.

All proposals for changes will be discussed by the WHO International Working Group for Drug Statistics Methodology.

The steps in the evaluation procedure for changes to DDDs are the same as the procedures for changes to ATC classifications (see page 38-39).

2. Data requirements for submission

When requesting changes of DDDs, the data requirements are similar to the data required for new DDDs. An important basis for the ATC/DDD system is to maintain a stable database for drug consumption studies. Because of this, there need to be compelling reasons to change DDDs. Conclusive arguments might be:

- a change in the main indication so that the average dose used has been altered.
- a large change (in the order of 50 %) in the average dose used (see also page 23). This would need to be supported by detailed market research data in a range of countries including developing countries. However, for the three year revision a smaller change can be accepted (see page 29).

Minor changes in DDD for reimbursement, pricing or marketing purposes will not be considered.

VI. DESCRIPTION OF ATC INDEX WITH DDDs

The WHO Collaborating Centre for Drug Statistics Methodology publishes a new issue of the complete **ATC index with DDDs** annually. The complete ATC index consists of one list sorted according to ATC codes, including all the established ATC codes and DDDs for plain substances, and one list alphabetically sorted according to nonproprietary drug names, including all ATC 5th levels. A searchable version of the index is available on the website www.whocc.no. The search options enable the user to find ATC codes and DDDs based on substance name or ATC levels. Text from the *Guidelines for ATC classification and DDD assignment* linked to the ATC level is also available. The text will give information related to the background for the ATC and DDD assignment. The complete ATC index can also be ordered from the Centre as a paper copy or as an electronic version. A pdf document of the *Guidelines* is available on our website.

The DDDs, which are to be reviewed during the year, are marked with an asterisk in the ATC index.

Lists of the annual ATC/DDD alterations and new ATC/DDDs are available in December each year on our website www.whocc.no. The lists are distributed free of charge by email to the users of the ATC/DDD system that are included on the Centre's mailing list.

Cumulative lists of ATC/DDD alterations performed since 1982 are available on our website www.whocc.no.

List of DDDs for combined products where the assigned DDD deviates from the general principles is available on our website www.whooc.no.

VII. OTHER ATC CLASSIFICATION SYSTEMS

A. ATCvet classification

The Anatomical Therapeutic Chemical classification for veterinary medicinal products, ATCvet, is based on the same main principles as the ATC system for medicines for human use. The ATCvet classification is kept as close to the human system as possible, but with special adaptations in order to make it suitable for veterinary medicines. The ATCvet classification was developed by the Nordic Council on Medicines, and was taken over by the WHO Collaborating Centre for Drug Statistics Methodology in January 2001. Further information on the ATCvet classification can be found on our website www.whooc.no.

B. ATC herbal classification

A framework for ATC classification of herbal remedies was developed by Dr. Peter De Smet, The Netherlands, in 1998. The classification is structurally similar to the official ATC system, but the herbal classification is not adopted by WHO. The Uppsala Monitoring Centre is responsible for the ATC herbal classification, and it is used in their Drug Dictionary.

The Uppsala Monitoring Centre has published Guidelines for Herbal ATC (HATC) classification and a Herbal ATC Index. The Herbal ATC Index includes a list of accepted scientific names with HATC codes, while the guideline is intended to help in assigning HATC codes to herbal remedies.

Further information about the Herbal ATC classification can be obtained from Dr Mohamed Farah [address: The Uppsala Monitoring Centre (WHO Collaborating Centre for International Drug Monitoring), Box 1051, S-751 40 Uppsala, Sweden, E-mail: Mohamed.farah@who-umc.org].

VIII. ATC/DDD INTERPRETATIVE GUIDELINES

This book includes all ATC headings down to the 4th level.

The comments included vary from one ATC group to another. No comments are given if the establishment of ATC codes and DDDs is considered to cause no special problems.

Comments related to the assignment of DDDs are given in shadowed boxes.

The interpretative guidelines that follow should be consulted whenever the ATC/DDD system is used for drug utilization research. They describe particular issues that were discussed and resolved by consensus of the Working Group during deliberation while establishing ATC/DDDs. If no special problems or issues arose during that process, no comments are given.

ATC SYSTEM MAIN GROUPS

The main groups of the ATC classification system are listed below. A survey of each main group is given in the beginning of each of the following chapters.

- A Alimentary tract and metabolism
- B Blood and blood forming organs
- C Cardiovascular system
- D Dermatologicals
- G Genito urinary system and sex hormones
- H Systemic hormonal preparations, excl. sex hormones and insulins
- J Antiinfectives for systemic use
- L Antineoplastic and immunomodulating agents
- M Musculo-skeletal system
- N Nervous system
- P Antiparasitic products, insecticides and repellents
- R Respiratory system
- S Sensory organs
- V Various

A ALIMENTARY TRACT AND METABOLISM

A01 STOMATOLOGICAL PREPARATIONS

A Stomatological preparations

A02 DRUGS FOR ACID RELATED DISORDERS

A Antacids

B Drugs for peptic ulcer and gastro-oesophageal reflux disease (GORD)

X Other drugs for acid related disorders

A03 DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS

A Drugs for functional bowel disorders

B Belladonna and derivatives, plain

C Antispasmodics in combination with psycholeptics

D Antispasmodics in combination with analgesics

E Antispasmodics and anticholinergics in combination with other drugs

F Propulsives

A04 ANTIEMETICS AND ANTINAUSEANTS

A Antiemetics and antinauseants

A05 BILE AND LIVER THERAPY

A Bile therapy

B Liver therapy, lipotropics

C Drugs for bile therapy and lipotropics in combination

A06 LAXATIVES

A Laxatives

A07 ANTIDIARRHEALS, INTESTINAL ANTIINFLAMMATORY/ ANTIINFECTIVE AGENTS

A Intestinal antiinfectives

B Intestinal adsorbents

C Electrolytes with carbohydrates

D Antipropulsives

E Intestinal antiinflammatory agents

F Antidiarrheal microorganisms

X Other antidiarrheals

- A08** **ANTI-OBESITY PREPARATIONS, EXCL. DIET PRODUCTS**
A *Antiobesity preparations, excl. diet products*
- A09** **DIGESTIVES, INCL. ENZYMES**
A *Digestives, incl. enzymes*
- A10** **DRUGS USED IN DIABETES**
A *Insulins and analogues*
B *Blood glucose lowering drugs, excl. insulins*
X *Other drugs used in diabetes*
- A11** **VITAMINS**
A *Multivitamins, combinations*
B *Multivitamins, plain*
C *Vitamin A and D, incl. combinations of the two*
D *Vitamin B₁, plain and in combination with vitamin B₆ and B₁₂*
E *Vitamin B-complex, incl. combinations*
G *Ascorbic acid (vitamin C), incl. combinations*
H *Other plain vitamin preparations*
J *Other vitamin products, combinations*
- A12** **MINERAL SUPPLEMENTS**
A *Calcium*
B *Potassium*
C *Other mineral supplements*
- A13** **TONICS**
A *Tonics*
- A14** **ANABOLIC AGENTS FOR SYSTEMIC USE**
A *Anabolic steroids*
B *Other anabolic agents*
- A15** **APPETITE STIMULANTS**
- A16** **OTHER ALIMENTARY TRACT AND METABOLISM PRODUCTS**
A *Other alimentary tract and metabolism products*

A ALIMENTARY TRACT AND METABOLISM

A01 STOMATOLOGICAL PREPARATIONS

A01A STOMATOLOGICAL PREPARATIONS

This group comprises agents for treatment of conditions of mouth and teeth. It is difficult to differentiate between preparations for use in the mouth and preparations for use in the throat. Preparations mainly used in gingivitis, stomatitis etc. should be classified in this group.

Preparations for the treatment of throat infections, (lozenges for common cold conditions) are classified in R02 - *Throat preparations*.

Preparations containing local anesthetics, see N01B - *Anesthetics, local*, and R02AD - *Anesthetics, local*.

A01AA Caries prophylactic agents

This group comprises all types of fluoride preparations (tablets, gargles, toothpastes, chewing-gum etc.).

Combinations of olaflur and dectaflur are classified at the 5th level of olaflur - A01AA03. Combinations of sodium fluoride and sodium monofluorophosphate are classified in A01AA30.

For caries prophylactic agents in A01AA, the DDDs are based on use in children. DDDs are only established for tablets.

A01AB Antiinfectives and antiseptics for local oral treatment

This group comprises all antiinfective and antiseptic agents for the treatment of stomatitis, gingivitis etc. Products used in common minor infections of mouth and throat are classified in R02, e.g. cetylpyridinium.

Other antibiotics for local use, see D - *Dermatologicals*.

The DDD for amphotericin in this group refers to lozenges.

The DDD for minocycline is based on the amount of active substance used in one periodontal pocket in local treatment of periodontitis.

A01AC Corticosteroids for local oral treatment

This group comprises corticosteroid preparations for the treatment of gingivitis, stomatitis etc., i.e. corticosteroid preparations for use in the oral cavity.

Combinations of corticosteroids and local anesthetics are classified here.

Other corticosteroids for local use, see D - *Dermatologicals*.

No DDDs have been established in this group. The dosage forms are mainly ointments and pastes.

A01AD Other agents for local oral treatment

This group comprises e.g. various gargles and hemostatic agents used in dentistry.

Becaplermin in a kit for implantation indicated to treat periodontally related defects is classified here.

Other hemostatic agents, see B02BC - *Local hemostatics*.

E.g. combinations with local anesthetics for oral treatment are classified at the *various* level A01AD11.

See also N01B - *Anesthetics, local*.

No DDDs have been established in this group. The dosage forms are mainly ointments and pastes.

A02 DRUGS FOR ACID RELATED DISORDERS

A02A ANTACIDS

This group comprises plain antacid drugs, antacids in combination with antifatulents and antacids in combination with other drugs.

Antacids in combination with liquorice root or linseed are classified in this group.

Plain antifoatulents, see A03AX - *Other drugs for functional bowel disorders*.

The DDDs for antacids are based on treatment of hyperacidity and dyspepsia, not ulcer. One exception, however, is antacids in combination with antispasmodics in A02AG, where the DDDs are based on treatment of ulcer.

For ordinary salt combinations in A02AD, fixed doses are used instead of individual doses for every single preparation (10 tablets = 10 UD; 50 ml mixture = 10 UD).

A02AA Magnesium compounds

Magnesium carbonate used for treatment of mineral deficiency is classified here.

Combinations of different magnesium compounds are classified in A02AA10 - *combinations*.

A02AB Aluminium compounds

Combinations of different aluminium compounds are classified in A02AB10 - *combinations*.

A02AC Calcium compounds

Combinations of different calcium compounds are classified in A02AC10 - *combinations*.

A02AD Combinations and complexes of aluminium, calcium and magnesium compounds

Antacids with two or more of the substances in combination are classified here.

Ordinary salt combinations are classified at the same 5th level A02AD01 e.g. combinations of aluminium hydroxide, magnesium carbonate gel and attapulgit, while the various complexes with a layer structure are classified at separate 5th levels e.g. magaldrate and almagate.

A02AF Antacids with antiflatulents

A02AG Antacids with antispasmodics

Preparations containing a combination of antacids and antispasmodics are classified in this group if the main use is as an antacid. See also A03 - *Drugs for functional gastrointestinal disorders*.

A02AH Antacids with sodium bicarbonate

All antacids containing sodium bicarbonate are classified in this group.

No ATC 5th levels are assigned in this group.

Preparations containing sodium bicarbonate to be used only in connection with double-contrast radiography are classified in V07AY.

A02AX Antacids, other combinations

A02B DRUGS FOR PEPTIC ULCER AND GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)

Peptic ulcer includes ulcers in the oesophagus, stomach or duodenum.

Combinations with H₂-receptor antagonists are classified in A02B.

See also A03 - *Drugs for functional gastrointestinal disorders*. Antacids in combination with liquorice root or linseed are classified in A02A - *Antacids*.

Combinations with NSAIDs are classified in M01A.

A02BA H₂-receptor antagonists

Ranitidine bismuth citrate is classified here, whereas other bismuth salts are classified in A02BX.

The DDDs are based on treatment of peptic ulcers.

A02BB Prostaglandins

A02BC Proton pump inhibitors

The DDDs are based on treatment of gastro-oesophageal reflux disease.

A02BD Combinations for eradication of Helicobacter pylori

This group comprises fixed combination packages.

The DDDs for combination packages in this group are given a fixed dose DDD, e.g. 6 tablets per day gives a DDD = 6 UD.

A02BX Other drugs for peptic ulcer and gastro-oesophageal reflux disease (GORD)

Ranitidine bismuth citrate is classified in A02BA.

Alginic acid in combination with antacids (e.g. aluminium hydroxide, calcium carbonate) is given the code A02BX13.

The DDD for alginic acid in combination with antacids (A02BX13) is given in a fixed doses (10 tablets = 10 UD; 50 ml mixture = 10 UD).

A02X OTHER DRUGS FOR ACID RELATED DISORDERS

This group comprises preparations, which cannot be classified in the preceding groups.

A03 DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS

A major part of the preparations in this group are combined preparations. Preparations containing e.g. analgesics and antispasmodics could be classified either in this group or in N02 - *Analgesics*. Combinations of psycholeptics and antispasmodics could be classified in A03 or in N05 - *Psycholeptics* etc. The main indication for the use of the

combination will, together with the relative effect of the active components, decide the classification. In the treatment of pain caused by spasms, the spasmolytic component must be judged as more important than the analgesic component. Accordingly, analgesic/antispasmodic combinations should be classified in A03 if the main effect of the preparation is the antispasmodic action.

Combined preparations are classified in:

A03C - *Antispasmodics in combination with psycholeptics*

A03D - *Antispasmodics in combination with analgesics*

A03E - *Antispasmodics and anticholinergics in combination with other drugs*

Antispasmodics, which are used specifically in the urogenital tractus, are classified in G04BD - *Urinary antispasmodics*.

The DDD is equal for different routes of administration (oral, parenteral or rectal) of the same compound and is based on the oral dose.

A03A DRUGS FOR FUNCTIONAL BOWEL DISORDERS

Semisynthetic derivatives such as butylscopolamine, are classified in A03B - *Belladonna and derivatives, plain*.

Lubiprostone is classified in A06AX - *Other laxatives*.

Peripheral opioid receptor antagonists are classified in A06AH.

A03AA *Synthetic anticholinergics, esters with tertiary amino group*

A03AB *Synthetic anticholinergics, quaternary ammonium compounds*

Plain preparations containing glycopyrronium are classified in this group. Preparations containing glycopyrronium in combination with neostigmine are classified in N07AA51. Trospium see G04BD and A03DA.

A03AC *Synthetic antispasmodics, amides with tertiary amines*

A03AD Papaverine and derivatives

Combinations with sterculia are classified here. Systemic combinations containing papaverine are classified at the plain level for papaverine. Papaverine used for treatment of erectil dysfunction, see G04BE.

A03AE Drugs acting on serotonin receptors

A03AX Other drugs for functional bowel disorders

This group comprises all other drugs for functional bowel disorders, which cannot be classified in the preceding groups.

Combinations of silicones and antispasmodics are classified in A03AX13 if the main indication is flatulence.

Combinations of silicones and antacids are classified in A02AF.

Combinations of silicones and antipropulsives are classified in A07DA.

Trimethylphloroglucinol and combinations with trimethylphloroglucinol are allowed at the 5th level A03AX12 - *phloroglucinol*.

Dimeticone is classified in A03AX13 - *silicones*

A03B BELLADONNA AND DERIVATIVES, PLAIN

A03BA Belladonna alkaloids, tertiary amines

A03BB Belladonna alkaloids, semisynthetic, quaternary ammonium compounds

Combinations with codeine are classified in N02AA.

A03C ANTISPASMODICS IN COMBINATION WITH PSYCHOLEPTICS

Antispasmodics in combination with psycholeptics and other drugs (excl. analgesics) are classified in this group.

Antispasmodics in combination with both psycholeptics and analgesics are classified in A03EA.

The classification at the 5th levels is based on the antispasmodic component. At each 5th level several psycholeptics may occur. When classifying such combined products, it is necessary to look at the main indication and the composition, to see if the preparation should be classified in A03 or in N05 - *Psycholeptics* (see comments under A03).

A03CA Synthetic anticholinergic agents in combination with psycholeptics

General comments, see A03C.

Combinations with more than one antispasmodic substance are classified in a ranking according to the ATC code. A substance classified in A03CA01 takes precedence over a substance classified in A03CA02 etc.

A03CB Belladonna and derivatives in combination with psycholeptics

General comments, see A03C.

Combinations with more than one antispasmodic are classified in a ranking according to the ATC code. A substance classified in A03CB01 takes precedence over a substance classified in A03CB02 etc.

A03CC Other antispasmodics in combination with psycholeptics

This group comprises combined preparations with psycholeptics, which are not covered by A03CA and A03CB.

A03D ANTISPASMODICS IN COMBINATION WITH ANALGESICS

This group is completely parallel to A03C.

The classification at the 5th levels is based on the antispasmodic component. At each 5th level several analgesics may occur. Antispasmodics in combination with analgesics and other drugs (excl. psycholeptics) are classified in this group.

When classifying these combination products, it is necessary to look at the indications and the composition to see if the preparation should be classified in A03 or in N02 - *Analgesics*.

Opioid analgesics in combination with antispasmodics, see N02AG - *Opioids in combination with antispasmodics*. Ethylmorphine is not

regarded as a narcotic in this context.

Antispasmodics in combination with psycholeptics and analgesics are classified in A03EA.

A03DA Synthetic anticholinergic agents in combination with analgesics

General comments, see A03D.

Combinations with more than one antispasmodic are classified in a ranking according to the ATC code. A substance classified in A03DA01 takes precedence over a substance classified in A03DA02 etc.

Combinations containing codeine are classified here, provided the codeine content is less than 20 mg. See also N02AA.

Combinations of trospium and analgesics are classified here.

A03DB Belladonna and derivatives in combination with analgesics

General comments, see A03D.

Combinations with more than one antispasmodic are classified in a ranking according to the ATC code. A substance classified in A03DB01 takes precedence over a substance classified in A03DB02 etc.

A03DC Other antispasmodics in combination with analgesics

This group comprises combined preparations with analgesics, which are not covered by A03DA and A03DB.

A03E ANTISPASMODICS AND ANTICHOLINERGICS IN COMBINATION WITH OTHER DRUGS

General comments, see A03.

This group comprises all combined preparations with antispasmodics and anticholinergics, which are not covered by A03C or A03D.

A03EA Antispasmodics, psycholeptics and analgesics in combination

Antispasmodics in combination with psycholeptics, analgesics and other agents are classified in this group.

A03ED Antispasmodics in combination with other drugs

A03F PROPULSIVES

A03FA Propulsives

Agents stimulating gastro-intestinal motility are classified here, e.g. substituted benzamides.

Trimebutine is classified in A03AA.

A04 ANTIEMETICS AND ANTINAUSEANTS

A04A ANTIEMETICS AND ANTINAUSEANTS

Antihistamines, which are often used as antiemetics, are classified in R06 - *Antihistamines for systemic use*.

Metoclopramide is classified in A03FA.

Combinations with analgesics are classified in N02 - *Analgesics*.

Antivertigo preparations, see N07C.

A04AA Serotonin (5HT₃) antagonists

The DDDs are based on antiemetic treatment. The DDD for palonosetron is based on single dose treatment.

A04AD Other antiemetics

Fosaprepitant, a prodrug of aprepitant, is classified together with the parent drug in A04AD12.

The DDD for scopolamine plaster is one plaster (i.e. 1 UD). This DDD is based on prophylaxis of motion sickness.

DDDs for other substances classified in this group are based on antiemetic treatment.

The parenteral DDD for aprepitant (expressed as fosaprepitant) is based on the average daily dose in a three days combined parenteral/oral course.

A05 BILE AND LIVER THERAPY

A05A BILE THERAPY

A05AA Bile acid preparations

Preparations classified in this group are primarily bile acid preparations, but various combinations, e.g. with spasmolytics, can also be included in each 5th level.

A05AB Preparations for biliary tract therapy

A05AX Other drugs for bile therapy

This group comprises other drugs for bile therapy, which cannot be classified in the preceding groups.

A05B LIVER THERAPY, LIPOTROPICS

A05BA Liver therapy

Tioctic acid is classified in A16AX.

Preparations containing silibinin are classified at the same ATC 5th level as silymarin.

A05C DRUGS FOR BILE THERAPY AND LIPOTROPICS IN COMBINATION

A06 LAXATIVES

A06A LAXATIVES

Laxatives are mainly grouped according to their mode of action. All enemas are classified in A06AG, regardless of mode of action.

Some combination products are classified at separate levels. These are mentioned in the respective ATC group.

Otherwise combination products are classified at separate 5th levels using the corresponding 50-series.

Laxatives in combination with centrally acting antiobesity agents are classified in A08A - *Antiobesity preparations, excl. diet products*.

A06AA *Softeners, emollients*

This group comprises preparations containing liquid paraffin, docusate sodium etc. Docusate potassium is classified at the same 5th level as docusate sodium.

Combinations with contact laxatives are classified in A06AB, except all liquid paraffin combinations, which are classified in A06AA.

DDD for e.g. liquid paraffin and castor oil are given using the following unit: g (gram), (1 g = 1 ml for all practical purposes). Preparations classified in A06AA51 - *liquid paraffin, combinations*, are all given the same DDD = 3 UD (15 ml), independent of liquid paraffin concentration.

A06AB *Contact laxatives*

This group comprises agents, which mainly inhibit the absorption of electrolytes and water through a specific pharmacological mechanism.

Combinations with osmotically acting laxatives are classified here.

Combinations with bulk producing laxatives are classified in A06AC - *Bulk producers*.

Gas producing rectal preparations and glycerol suppositories, see A06AX - *Other laxatives*.

Phenolphthalein in combination with liquid paraffin, see A06AA.
Combined packages with tablets and enemas are classified in A06AG.

A major part of the products classified in this group are various combinations of two or more contact laxatives. These are classified at separate 5th levels:

A06AB20 - *contact laxatives in combination*

A06AB30 - *contact laxatives in combination with belladonna alkaloids*

Otherwise combination products are classified at separate 5th levels using the corresponding 50-series.

A06AC Bulk producers

This group comprises linseed and psylla seed products, methyl cellulose etc.

Lactulose, see A06AD.

Products containing linseed in combination with antacids are classified in A02A.

Products containing sterculia in combination with alverine are classified in A03AX.

A06AD Osmotically acting laxatives

This group comprises various saline purgatives and e.g. lactulose, which is primarily considered as an osmotically acting substance.

Combinations with contact laxatives are classified in A06AB.

Mineral salts in combinations are classified in A06AD10.

Combinations of lactulose with liquid paraffin should be classified in A06AD61.

Magnesium hydroxide is classified as an antacid in A02AA.

Magnesium in combination with albumin tannate are classified in A07XA.

The DDD for macrogol refers to macrogol 4000.

A06AG *Enemas*

All enemas and laxative rectal solutions are classified in this group, regardless of mode of action.

Combined packages containing tablets and enemas are classified in this group.

Some 5th levels for plain substances also include combinations, e.g.:

A06AG10 - docusate sodium- and e.g. sorbitol or glycerol

A06AG11 - laurilsulfate and e.g. sodium citrate

The DDDs for enemas classified in this group are 1 enema.

A06AH *Peripheral opioid receptor antagonists*

A06AX *Other laxatives*

This group comprises all laxatives, which cannot be classified in A06AA-A06AH, e.g. glycerol suppositories and carbon dioxide producing agents.

A07 **ANTIDIARRHEALS, INTESTINAL ANTIINFLAMMATORY/ANTIINFECTIVE AGENTS**

A07A **INTESTINAL ANTIINFECTIVES**

This group comprises locally acting antiinfectives. Antiinfectives for systemic use, see J - *Antiinfectives for systemic use*.

See also P - *Antiparasitic products, insecticides and repellents*.

A07AA *Antibiotics*

Vancomycin and colistin for oral therapy are classified in this group as they are used in enterocolitis. Vancomycin injection/infusion is classified in J01XA - *Glycopeptide antibacterials*, and colistin injection/infusion in J01XB - *Polymyxins*.

Most of the combined products containing more than one antibiotic, contain neomycin. Neomycin is given classification priority, thus all

combined products containing neomycin and other antibiotics should be classified in A07AA51 - *neomycin, combinations*.

The DDDs are based on treatment of intestinal infections.

A07AB Sulfonamides

The DDDs are based on preoperative prophylaxis of intestinal infections.

A07AC Imidazole derivatives

The DDDs are based on treatment of gastrointestinal mycosis.

A07AX Other intestinal antiinfectives

This group comprises antiinfectives, which cannot be classified in A07AA-C.

A07B INTESTINAL ADSORBENTS

Combinations with intestinal antiinfectives are classified in A07A.

A07BA Charcoal preparations

The DDD for charcoal preparations is based on treatment of common diarrhea.

A07BB Bismuth preparations

See also A02BX - *Other drugs for peptic ulcer and gastro-oesophageal reflux disease (GORD)*.

No ATC 5th levels are assigned in this group.

A07BC Other intestinal adsorbents

This group comprises all other intestinal adsorbents.

Combinations with albumin tannate are classified in A07XA.

A07C ELECTROLYTES WITH CARBOHYDRATES

A07CA *Oral rehydration salt formulations*

The DDDs are mainly based on use in children.

A07D ANTIPROPULSIVES

A07DA *Antipropulsives*

This group comprises agents which reduce gastrointestinal motility, e.g. diphenoxylate and loperamide. Loperamide and loperamide oxide are classified at the two separate 5th levels.

A07DA01 - *diphenoxylate* - includes combinations with atropine

A07DA02 - *opium* - includes also combinations with belladonna and/or bismuth subgallate, albumin etc.

Combinations with antifatulents are classified here.

The DDDs are based on treatment of acute diarrhea.

A07E INTESTINAL ANTIINFLAMMATORY AGENTS

A07EA *Corticosteroids acting locally*

Enemas and rectal foams for treatment of e.g. ulcerative colitis are classified here. Oral budesonide for treatment of morbus Crohn is also classified here.

The DDDs are given as 1 enema. The DDD for hydrocortisone rectal foam is given in amount of active substance.

The DDD for oral budesonide is based on the treatment of morbus Crohn.

A07EB Antiallergic agents, excl. corticosteroids

Cromoglicic acid for oral use in food allergy is classified in this group.

The DDD is based on treatment of food allergy.

A07EC Aminosalicylic acid and similar agents

Some preparations classified in this group are also used for treatment of rheumatoid arthritis.

The DDDs are based on treatment of colitis ulcerosa and morbus Crohn.

A07F ANTIDIARRHEAL MICROORGANISMS

A07FA Antidiarrheal microorganisms

Preparations with e.g. lactic acid producing organisms are classified in this group.

The DDDs are given in UDs (e.g. numbers of tablets).

A07X OTHER ANTIDIARRHEALS

A07XA Other antidiarrheals

Combinations with pectin and magnesium peroxide are classified here.

A08 ANTI-OBESITY PREPARATIONS, EXCL. DIET PRODUCTS

A08A ANTI-OBESITY PREPARATIONS, EXCL. DIET PRODUCTS

Low-energy diets, see V06AA.

A08AA Centrally acting antiobesity products

Centrally acting drugs mainly used to produce anorexia are classified in this group. Amphetamine, which is commonly used in psychiatry, is classified in N06B - *Psychostimulants, agents used for ADHD and nootropics*.

A08AB Peripherally acting antiobesity products

A08AX Other antiobesity drugs

A09 DIGESTIVES, INCL. ENZYMES

A09A DIGESTIVES, INCL. ENZYMES

A09AA Enzyme preparations

Only enzymes used in digestion disorders are classified in this group. Other enzymes, see B06AA - *Enzymes*, and D03BA - *Proteolytic enzymes*.

Enzyme preparations, which are indicated to treat inflammatory conditions, are classified in M09AB - *Enzymes*.

Combinations of digestive enzymes and other agents (e.g. silicone compounds and spasmolytics) are classified in this group if the main indication is digestion disorders.

Cholagogues are classified in A05 - *Bile and liver therapy*.

DDD's can be difficult to establish because of great variations in enzyme content. The DDD's are based on average recommended doses given in different drug catalogues. Most of the preparations are combinations of different enzymes, and the DDD's are therefore given in UD's. Some specific products have been given a DDD, see list of DDD's for combination products, www.whocc.no.

A09AB Acid preparations

A09AC Enzyme and acid preparations, combinations

A10 DRUGS USED IN DIABETES

A10A INSULINS AND ANALOGUES

This group comprises both human - and animal insulins.

Insulin preparations are classified at 4 different 4th levels, according to onset and duration of action. Each 4th level is differentiated in 5th levels according to origin of insulin.

Products consisting of, e.g. beef and pork insulin, are classified as combinations (30-levels) at each 4th level according to onset and duration of action.

The DDD for insulins is 40 units.

A10AB Insulins and analogues for injection, fast-acting

A10AC Insulins and analogues for injection, intermediate-acting

A10AD Insulins and analogues for injection, intermediate-acting combined with fast-acting

A10AE Insulins and analogues for injection, long-acting

A10AF Insulins and analogues for inhalation

A10B BLOOD GLUCOSE LOWERING DRUGS, EXCL. INSULINS

A10BA *Biguanides*

A10BB *Sulfonamides, urea derivatives*

The DDD for micronized glibenclamide is lower compared to non-micronized formulations, due to higher bioavailability.

The DDD for gliclazide is based on the modified release formulation.

A10BC *Sulfonamides (heterocyclic)*

A10BD *Combinations of oral blood glucose lowering drugs*

It has been considered most appropriate to assign fixed DDDs based on the average use of the different combinations without considering and comparing the strengths of the various components. 1 tablet is the fixed DDD for products given once daily whereas the fixed DDD for products given twice daily is 2 tablets. The assigned DDDs cannot always be compared with the DDDs assigned for plain preparations.

See list of DDDs for combined products, www.whocc.no

A10BF *Alpha glucosidase inhibitors*

A10BG *Thiazolidinediones*

The DDD for troglitazone is based on combination therapy. The DDDs for rosiglitazone and pioglitazone are based on monotherapy.

A10BH *Dipeptidyl peptidase 4 (DPP-4) inhibitors*

A10BX *Other blood glucose lowering drugs, excl. insulins*

All oral formulations of bromocriptine are classified in G02CB01.

A10X OTHER DRUGS USED IN DIABETES

A10XA *Aldose reductase inhibitors*

A11 VITAMINS

Vitamins constitute a comprehensive group of therapeutic and prophylactic preparations. Before classifying any product it is important to be familiar with the main subdivision of the group.

It may be necessary to consider whether a product is a vitamin preparation with iron or an iron preparation with vitamins, a mineral preparation with vitamins or a vitamin preparation with minerals, or if the product should be regarded as a tonic etc. As an aid to such considerations, guidelines are given at each sublevel.

Vitamin B₁₂ is classified in B03 - *Antianemic preparations*.

Vitamin K is classified in B02 - *Antihemorrhagics*.

Vitamins administered as i.v. solution additives, see B05XC.

Some definitions:

Multivitamins: Products containing minimum vitamins A, B, C and D. One B-vitamin is sufficient.

B-complex: Products containing minimum thiamine, riboflavine, pyridoxine, nicotinamide. The products may contain other B-vitamins.

A11A MULTIVITAMINS, COMBINATIONS

The DDDs are based on prophylaxis. For simplicity, the DDDs for oral formulations are given as fixed doses (1 tablet = 1 UD; 30 ml mixture = 6 UD).

A11AA *Multivitamins with minerals*

The group is subdivided:

A11AA01 - *multivitamins and iron*

A11AA02 - *multivitamins and calcium*

A11AA03 - *multivitamins and other minerals, incl. combinations*

A11AA04 - *multivitamins and trace elements*

In A11AA01, 02 and 03, combinations with trace elements are allowed.

In A11AA04 only trace elements are allowed in addition to multivitamins.

Combinations with other substances, e.g. caffeine, are classified in A11AB.

Cholin, biotin, inositol and para-amino benzoic acid are regarded as vitamins and are allowed in preparations classified in A11AA.

A11AA01 multivitamins and iron

Preparations containing multivitamins and sub-therapeutic doses of iron are classified in this group.

Sub-therapeutic doses of iron are defined as 5-30 mg of Fe^{2+} per defined daily dose, with corresponding limits for the various Fe^{3+} salts, if the main indication is not "iron deficiency". Preparations containing more than 30 mg Fe^{2+} (or corresponding doses of Fe^{3+}) are classified as iron preparations (B03A) regardless of therapeutic use.

See also A11AA.

A11AA02 multivitamins and calcium

Preparations containing multivitamins and sub-therapeutic doses of calcium are classified in this group, e.g. a calcium content of up to 500 mg calcium carbonate per tablet have been allowed.

See also A11AA.

Calcium preparations, see A12A.

A11AA03 multivitamins and other minerals, incl. combinations

Preparations containing multivitamins and sub-therapeutic doses of one or more mineral are classified in this group. Definitions of sub-therapeutic doses of iron and calcium, see A11AA01 and A11AA02.

See also A11AA.

Mineral supplements, see A12.

A11AA04 multivitamins and trace elements

Preparations containing multivitamins and trace elements are classified in this group. No other combinations should occur in this group.

A11AB Multivitamins, other combinations

This group comprises all combined preparations with multivitamins, which are not classified in A11AA.

Preparations containing caffeine, strychnine etc. are classified in this group.

Preparations containing cholin, biotin, inositol, para-amino benzoic acid etc. should be classified in A11AA.

A11B MULTIVITAMINS, PLAIN

A11BA Multivitamins, plain

Only plain multivitamin preparations are allowed.

The DDDs are based on prophylaxis. For simplicity, the DDDs are given as fixed doses (1 tablet = 1 UD; 30 ml mixture = 6 UD).

A11C VITAMIN A AND D, INCL. COMBINATIONS OF THE TWO

Combinations with trace elements are allowed. Other combinations, see A11J - *Other vitamin products, combinations*.

See also A12 - *Mineral supplements*.

A11CA Vitamin A, plain

The DDD is based on treatment of vitamin A deficiency.

A11CB Vitamin A and D in combination

Cod-liver oil products are classified in this group.

The DDDs are based on prophylaxis in children.

A11CC Vitamin D and analogues

Vitamin D and analogues may be regarded as hormones, but are classified in this group. Calcium homeostasis, see H05.

Paricalcitol and doxercalciferol indicated for the prevention and treatment of secondary hyperparathyroidism are classified in H05BX - *Other anti-parathyroid agents*.

The DDDs are based on therapeutic use. No DDDs are established for ergocalciferol and colecalciferol due to great differences between doses used for various indications.

A11D VITAMIN B₁, PLAIN AND IN COMBINATION WITH VITAMIN B₆ AND B₁₂

Combinations with trace elements are allowed. Other combinations see A11J - *Other vitamin products, combinations*.

A11DA Vitamin B₁, plain

The DDDs are based on treatment of vitamin B₁ deficiency.

A11DB Vitamin B₁ in combination with vitamin B₆ and/or vitamin B₁₂

Combinations with vitamin B₂ are also allowed in this group.

For vitamin B₁ in combination with vitamin B₆ and/or vitamin B₁₂, DDDs are only established for parenteral preparations, based on the volume of one ampoule. The DDDs are given in UD_s (1 UD = 1 ml).

A11E VITAMIN B-COMPLEX, INCL. COMBINATIONS

Definition of vitamin B-complex, see A11 - *Vitamins*.
The group is subdivided:

- A11EA - *Vitamin B-complex, plain*
- A11EB - *Vitamin B-complex with vitamin C*
- A11EC - *Vitamin B-complex with minerals*
- A11ED - *Vitamin B-complex with anabolic steroids*
- A11EX - *Vitamin B-complex, other combinations*

Combinations with trace elements are allowed. Vitamin B-complex in combination with other vitamins than vitamin C, see A11J - *Other vitamin products, combinations*.

DDDs are based on prophylaxis. DDDs are given as fixed doses (1 tablet = 1 UD; 30 ml mixture = 6 UD). DDDs for parenteral preparations are based on the volume of one ampoule. The DDDs for these preparations are given in UD (1 UD = 1 ml).

A11EA Vitamin B-complex, plain

This group comprises plain vitamin B-complex preparations, also in combination with liver extract. Liver extract preparations, see also B03BA - *Vitamin B₁₂ (cyanocobalamin and derivatives)*. See also A11E.

A11EB Vitamin B-complex with vitamin C

This group comprises all combinations of vitamin B-complex and vitamin C. Combinations with anabolic steroids, see A11ED.

See also A11E, A11E D and A11EX.

A11EC Vitamin B-complex with minerals

Preparations containing vitamin B-complex and sub-therapeutic doses of one or more mineral are classified in this group.

See also A11E.

Mineral supplements, see A12.

A11ED Vitamin B-complex with anabolic steroids

Preparations containing vitamin B-complex and anabolic steroids are

classified in this group. Even combinations containing vitamin C, minerals or other substances, e.g. caffeine are classified in this group.

A11EX Vitamin B-complex, other combinations

This group comprises preparations with vitamin B-complex (plain or in combination with vitamin C or minerals) and other substances, e.g. caffeine, strychnine.

A11G ASCORBIC ACID (VITAMIN C), INCL. COMBINATIONS

Other preparations with vitamin C, see A11EB - *Vitamin B-complex with vitamin C*, and A11J - *Other vitamin products, combinations*.

Combinations with analgesics are classified in N02B.

The DDD refers to the assumed daily requirement.
For combination products, the DDDs are given as fixed doses for all tablets (1 tablet = 1 UD).

A11GA Ascorbic acid (vitamin C), plain

Combinations with trace elements only, are allowed.

A11GB Ascorbic acid (vitamin C), combinations

This group comprises combinations with e.g. minerals.

Preparations containing ascorbic acid and calcium should be classified in A12AX - *Calcium, combinations with other drugs* - if they are used in calcium deficiency or osteoporosis.

A11H OTHER PLAIN VITAMIN PREPARATIONS

A11HA Other plain vitamin preparations

Vitamin B₁₂, see B03BA.

Vitamin K, see B02 - *Antihemorrhagics*.

Combinations with trace elements are allowed. Other combinations, see A11DB and A11J.

DDDs are established only for tocopherol, pyridoxine and nicotinamide, and refers to assumed daily requirement in vitamin deficiency.

A11J OTHER VITAMIN PRODUCTS, COMBINATIONS

The group is subdivided:

A11JA - *Combinations of vitamins*

A11JB - *Vitamins with minerals*

A11JC - *Vitamins, other combinations*

Combinations with trace elements are allowed.

The DDDs are given as fixed doses (1 tablet = 1 UD; 30 ml mixture = 6 UD), except for concentrated ACD vitamin drops.

A11JA Combinations of vitamins

This group comprises all combinations of vitamins with no addition of other substances, not covered by the preceding groups.

A11JB Vitamins with minerals

This group comprises all combinations of vitamins with minerals in sub-therapeutic doses, not covered by the preceding groups.

See also A12 - *Mineral supplements*.

A11JC Vitamins, other combinations

This group comprises all products, which contain vitamins (with or without minerals) and in addition other substances, e.g. caffeine and strychnine. Combinations with folic acid are classified in B03BB if "folic acid deficiency" is the main indication.

This group contains products, which may also be regarded as tonics. No sharp line has been drawn between these two groups.

Tonics are classified in A13. The vitamin content of tonics should be rather low.

A12 MINERAL SUPPLEMENTS

This group contains mineral supplements used for treatment of mineral deficiency. Magnesium carbonate used for treatment of mineral deficiency is classified in A02AA01.

A12A CALCIUM

A12AA *Calcium*

All plain calcium preparations, incl. bone extracts are classified in this group. See also B05X - *I.v. solution additives*.

Combinations of different calcium salts are given the following ATC code: A12AA20. Small amounts of calcium carbonate (i.e. 300 mg per tablet) are, however, allowed at each 5th level for plain calcium preparations.

The combination of calcium acetate and magnesium carbonate is classified in V03AE.

See also:

A11AA02 - *multivitamins and calcium*

A11EC - *Vitamin B-complex with minerals*

A11GB01 - *ascorbic acid (vit C) and calcium*

A11JB - *Vitamins with minerals*

The DDDs are based on treatment of calcium deficiency and osteoporosis.

A12AX *Calcium, combinations with other drugs*

This group comprises all combined calcium preparations used in the treatment of calcium deficiency conditions and osteoporosis. Many of these are combinations with vitamins, especially vitamin A and D.

Combination packages of calcium and bisphosphonates are classified in M05BB.

Combinations with fluoride are classified in A12CD.

A12B POTASSIUM

A12BA *Potassium*

This group comprises preparations used as potassium supplements.

This group comprises also all combined potassium preparations used in the treatment of potassium deficiency conditions.

Small non-therapeutic amounts of potassium hydrogencarbonate are allowed at each level of plain potassium salts.

Potassium, combinations with other drugs, are classified at separate 5th levels using the corresponding 50-series.

Diuretics and potassium in combination, see C03 - *Diuretics*.

See also B05 - *Blood substitutes and perfusion solutions*.

The DDDs are based on treatment of potassium deficiency and correspond to a potassium content of about 40 mmol potassium.

A12C OTHER MINERAL SUPPLEMENTS

This group comprises other minerals.

See also B05 - *Blood substitutes and perfusion solutions*.

A12CA *Sodium*

The DDD has been set to 1 g NaCl.

A12CB *Zinc*

The DDD is based on treatment of zinc deficiency.

A12CC Magnesium

The DDDs for the various magnesium salts are equivalent to an assumed daily requirement of 300 mg Mg (oral dose). The DDD for some of the oral formulations are higher than the parenteral formulations due to lower bioavailability.

A12CD Fluoride

This group comprises preparations used e.g. in the treatment of osteoporosis. Fluoride used in caries prophylaxis, see A01AA - *Caries prophylactic agents*.

Bisphosphonates are classified in M05B.
Calcitonin is classified in H05BA.
Calcium preparations are classified in A12A.
Combinations with calcium are classified here.

The DDD is based on treatment of osteoporosis.

A12CE Selenium

The DDDs are based on treatment of selenium deficiency and is expressed as amount of selenium (Se).

A12CX Other mineral products

A13 TONICS

A13A TONICS

This group comprises preparations used as tonics etc., if preparations do not fill the requirements to be classified as iron preparations, vitamin preparations etc.

All mixtures classified in this group are given a fixed DDD (30 ml = 6 UD).

A14 ANABOLIC AGENTS FOR SYSTEMIC USE

A14A ANABOLIC STEROIDS

Anabolic steroids are subdivided in different 4th levels according to chemical structure.

Anabolic steroids used exclusively in cancer therapy, see
L - Antineoplastic and immunomodulating agents.

The DDDs are based on e.g. treatment of anemia.

A14AA Androstan derivatives

A14AB Estren derivatives

A14B OTHER ANABOLIC AGENTS

This group comprises all other anabolic agents which cannot be classified in the preceding groups.

A15 APPETITE STIMULANTS

This group comprises preparations only used as appetite stimulants. A number of drugs with other main actions may have appetite stimulating properties.

Cyproheptadine, also used as an appetite stimulant in children, is classified in R06AX. Pizotifen is classified in N02CX.

No DDDs are established in this group.

A16 OTHER ALIMENTARY TRACT AND METABOLISM PRODUCTS

A16A OTHER ALIMENTARY TRACT AND METABOLISM PRODUCTS

This group comprises all products acting on the alimentary tract and metabolism which cannot be classified in the preceding groups. V03 - *All other therapeutic products*, should also be considered.

Nutrients are classified in V06 - *General nutrients*.

A16AA Amino acids and derivatives

Agents used in various metabolic deficiency states are classified here, when this is considered to be the main indication e.g. levocarnitine. Tryptophan and oxitriptan are classified in N06A.

The DDD of levocarnitine is based on treatment of primary carnitine deficiency.

A16AB Enzymes

A16AX Various alimentary tract and metabolism products

Tioctic acid is classified here.

The DDD for zinc acetate is expressed as the amount of zinc (Zn). The DDD for nitisinone is based on the treatment of children with a bodyweight of 20 kg.

B BLOOD AND BLOOD FORMING ORGANS

B01 ANTITHROMBOTIC AGENTS

A Antithrombotic agents

B02 ANTIHEMORRHAGICS

A Antifibrinolytics

B Vitamin K and other hemostatics

B03 ANTIANEMIC PREPARATIONS

A Iron preparations

B Vitamin B₁₂ and folic acid

X Other antianemic preparations

B05 BLOOD SUBSTITUTES AND PERFUSION SOLUTIONS

A Blood and related products

B I.v. solutions

C Irrigating solutions

D Peritoneal dialytics

X I.v. solution additives

Z Hemodialytics and hemofiltrates

B06 OTHER HEMATOLOGICAL AGENTS

A Other hematological agents

B BLOOD AND BLOOD FORMING ORGANS

B01 ANTITHROMBOTIC AGENTS

B01A ANTITHROMBOTIC AGENTS

B01AA Vitamin K antagonists

This group comprises vitamin K antagonists such as dicoumarol, warfarin etc.

The DDDs are based on prophylaxis of thrombosis.

B01AB Heparin group

This group comprises heparin preparations, including products for non-therapeutic use, e.g. for rinsing of indwelling vein cannulas. Heparin sodium and heparin calcium are classified at the same 5th level, i.e. B01AB01. The low molecular weight heparins are classified at separate 5th levels.

The DDDs of nonfractionated heparin and antithrombin are based on prophylaxis of thrombosis and pulmonary emboli, and given in international units (U). The DDDs for the different low molecular weight heparins are assigned according to their recommended dose in prophylaxis of deep vein thrombosis in moderate risk patients. Since the anti Xa activity is a major determinant of the anticoagulant activity of low molecular weight heparins the DDDs are given in international units based on anti Xa activity.

B01AC Platelet aggregation inhibitors excl. heparin

Acetylsalicylic acid preparations specifically intended for use as antithrombotic agents are classified in this group. This exception from the basic principle of only one code for each route of administration is made because of the extensive use of acetylsalicylic acid both as an antithrombotic agent and as an analgesic. Whether an acetylsalicylic acid product should be classified in this group or in N02BA, should be decided at the national level based on the main indication of the product.

Lysine acetylsalicylate is classified at the same 5th level as acetylsalicylic acid.

Sulfapyrazone is classified in M04AB. Alprostadil is classified in C01EA and G04BE.

Combinations of acetylsalicylic acid and statins are classified in C10B.

Combinations of ramipril, simvastatin, and acetylsalicylic acid are classified in C10BX.

The DDDs are based on prophylaxis of thrombosis. The DDDs of acetylsalicylic acid and carbasalate calcium are given as 1 tablet independent of tablet strength. This is due to the great variations between different countries in the dosages/strengths recommended for prophylaxis of thrombosis.

The DDD of iloprost is based on treatment of peripheral vascular disease.

For combinations products, see list of DDDs for combinations, www.whooc.no.

B01AD Enzymes

The DDDs of streptokinase, alteplase, anistreplase and reteplase are based on thrombolytic treatment in connection with acute myocardial infarction. The DDD of urokinase is based on treatment of acute lung emboli. The DDDs are either expressed in international units or gram.

B01AE Direct thrombin inhibitors

B01AX Other antithrombotic agents

B02 ANTIHEMORRHAGICS

B02A ANTIFIBRINOLYTICS

This group comprises agents, which inhibit fibrinolytic activity.

Combinations with vitamin K, see B02B - *Vitamin K and other hemostatics*.

The DDDs are based on treatment of hemorrhage associated with fibrinolysis.

B02AA Amino acids

B02AB Proteinase inhibitors

Combinations with aprotinin used as local hemostatics are classified in B02BC30.

B02B VITAMIN K AND OTHER HEMOSTATICS

The DDDs are based on treatment of hemorrhage associated with different deficiency states (e.g. vitamin K deficiency, deficiency of different blood coagulation factors etc.).

B02BA Vitamin K

B02BB Fibrinogen

Preparations containing human fibrinogen for systemic use are classified here. B02BB01 is reserved for systemic formulations only.

B02BC Local hemostatics

This group comprises gauze, tampons etc. impregnated with hemostatic agents. Local hemostatics used in dentistry, see A01AD - *Other agents for local oral treatment*. Epinephrine injection, see C01C - *Cardiac stimulants excl. cardiac glycosides*. Tissue adhesives, e.g. cyanoacrylate based adhesives, are classified in V03AK. Combination with aprotinin is allowed in B02BC30.

No DDDs are established for local hemostatics classified in this group.

B02BD Blood coagulation factors

This group comprises all blood coagulation factors, thrombin etc., incl. preparations for local use, and their combinations. Fibrinogen (factor I), see - B02BB - *Fibrinogen*.

The DDDs for the coagulation factor IX (B02BD04 and B02BD09) are in the lower end of the dose range.

B02BX Other systemic hemostatics

This group comprises systemic hemostatics, which cannot be classified elsewhere.

B03 ANTIANEMIC PREPARATIONS

B03A IRON PREPARATIONS

This group comprises all plain iron preparations and all combination products containing more than 30 mg Fe²⁺ (or corresponding amounts of Fe³⁺ salts) per defined daily dose (DDD) of the product, regardless of therapeutic use.

Combined preparations with 30 mg or less Fe²⁺ per DDD should be classified as vitamin preparations in group A11 or as tonics in group A13. All iron preparations with "iron deficiency" as the main indication are classified in B03A, regardless of the amount of iron salts.

Only plain preparations should be classified in the groups B03AA, B03AB and B03AC. Combinations with stabilizing agents (e.g. ascorbic acid) are allowed at each 5th level. Combinations with e.g. laxatives are classified at separate 5th levels by using the 50-series.

Other combinations, see B03AD and B03AE.

B03AA Iron bivalent, oral preparations

The DDDs are based on treatment of iron deficiency anemia. The DDDs are established according to amount of Fe^{2+} and are equal for all compounds regardless of iron salt (i.e. the DDD corresponds to 0.2 g Fe^{2+}).

B03AB Iron trivalent, oral preparations

The DDDs are based on treatment of iron deficiency anemia. Separate DDDs are established for the different trivalent iron salts. The DDDs are expressed in grams of Fe^{3+} .

B03AC Iron trivalent, parenteral preparations

Ferric carboxymaltose and dexترفerron are classified in B03AC01 - *ferric oxide polymaltose complexes*.

Various dextran complexes are classified in B03AC06 - *ferric oxide dextran complexes*.

The DDDs are based on treatment of iron deficiency anemia. The DDDs are established according to amount of Fe^{3+} and are equal for all compounds (i.e. the DDD corresponds to 0.1 g Fe^{3+}).

B03AD Iron in combination with folic acid

This group comprises iron in combination with folic acid. Preparations containing additional substances, see B03AE.

The DDDs should be based on prophylaxis of iron deficiency anemia and folic acid deficiency during pregnancy (i.e. about half the iron dose for treatment of anemia).

B03AE Iron in other combinations

This group comprises preparations, which in addition to iron or iron and folic acid contain other substances.

The group is subdivided:

- B03AE01 - *iron, vitamin B₁₂ and folic acid*
 Intrinsic factor and/or liver extract are also allowed in this group
- B03AE02 - *iron, multivitamins and folic acid*
- B03AE03 - *iron and multivitamins*
- B03AE04 - *iron, multivitamins and minerals*
- B03AE10 - *various combinations*
 This group comprises some "borderline" combined iron preparations i.e. preparations with an iron content of approximately 30 mg Fe²⁺ per defined daily dose (DDD).

For combinations of iron, vitamin B₁₂ and folic acid (B03AE01), the DDDs are based on prophylaxis of iron deficiency anemia and folic acid deficiency during pregnancy.

Various combinations, classified in B03AE10, contain very small amounts of iron. The DDDs for these combinations are based on dose recommendations, and can be as low as corresponding to 30 mg Fe²⁺.

The DDDs for iron in other combinations are based on treatment of iron deficiency anemia, and correspond to a DDD of 0.2 g Fe²⁺.

B03B VITAMIN B₁₂ AND FOLIC ACID

B03BA Vitamin B₁₂ (cyanocobalamin and analogues)

Hydroxocobalamin for treatment of neuralgia is classified here. Combinations with liver extract are classified at separate 5th levels using the corresponding 50-series. Combinations with folic acid are classified in this group by using the 50-series.

Vitamin B₁₂, see also:

- A11D - *Vitamin B₁, plain and in combination with vitamin B₆ and B₁₂*
- A11EA - *Vitamin B-complex, plain*
- B03A - *Iron preparations*

The DDDs are based on maintenance treatment of pernicious anemia. Different DDDs are assigned for oral and parenteral formulations of cyanocobalamin due to great differences in bio-availability.

The DDD for mecobalamin is based on the treatment of peripheral neuropathies.

B03BB Folic acid and derivatives

Folic acid and derivatives in combination with other substances are classified in this group at separate 5th levels using the corresponding 50-series, if folic acid deficiency is the main indication. Folinates, used as antidotes, are classified in V03A. Combinations with iron, see B03AD and B03AE.

Combinations with vitamin B₁₂ are classified in B03BA.

The DDD for oral folic acid is based on prophylactic use and the parenteral DDD is based on treatment.

B03X OTHER ANTIANEMIC PREPARATIONS

This group comprises antianemic preparations other than iron, vitamin B₁₂ and folic acid.

B03XA Other antianemic preparations

The DDDs are based on treatment of renal anemia in patients maintained by hemodialysis.

B05 BLOOD SUBSTITUTES AND PERFUSION SOLUTIONS

See also:

V07AB - *Solvents and diluting agents, incl. irrigating solutions*

V07AC - *Blood transfusion, auxiliary products*

No DDDs are established in this group. It is considered difficult to establish DDDs, because of the great variations in dosages given.

B05A BLOOD AND RELATED PRODUCTS

B05AA Blood substitutes and plasma protein fractions

Polygeline is classified in B05AA06 gelatin agents.

ATC level B05AA07 hydroxyethylstarch includes starches that have been etherified to varying extent e.g. hepta-, hexa-, penta-, and tetrastarches.

B05AX Other blood products

B05B I.V. SOLUTIONS

This group comprises i.v. solutions used in parenteral administration of fluids, electrolytes and nutrients. Agents administered as i.v. solutions or additives, see the respective therapeutic groups. I.v. solution additives, see B05X.

B05BA Solutions for parenteral nutrition

This group comprises amino acids, carbohydrates, fat emulsions etc. for parenteral nutrition. Combinations with electrolytes are allowed. Combinations of electrolytes and glucose are classified in B05BB - *Solutions affecting the electrolyte balance*. These and similar combinations are not primarily used as nutrients.

B05BB Solutions affecting the electrolyte balance

This group comprises electrolyte solutions, incl. combinations with e.g. carbohydrates. Combinations with amino acids, fat etc. should be classified in B05BA.

B05BC Solutions producing osmotic diuresis

B05C IRRIGATING SOLUTIONS

In this group products used for bladder irrigation, surgical irrigation, incl. instruments etc. are classified. See also V07AB - *Solvents and diluting agents, incl. irrigating solutions.*

Combined preparations are classified by using 5th level - 10. Only plain preparations are classified at the other 5th levels.

B05CA Antiinfectives

B05CB Salt solutions

B05CX Other irrigating solutions

B05D PERITONEAL DIALYTICS

B05DA Isotonic solutions

B05DB Hypertonic solutions

B05X I.V. SOLUTION ADDITIVES

I.v. solution additives are concentrated preparations containing substances used for correcting fluid and electrolyte balance and nutritional status. Drugs administered as i.v. solutions or additives, see the respective groups.

B05XA Electrolyte solutions

This group comprises plain electrolyte solutions, combinations of electrolytes, and combinations of electrolytes and other substances (e.g. trace elements). Electrolytes in combination with trace elements, are classified in B05XA31.

See also A12 - *Mineral supplements.*

B05XB Amino acids

B05XC Vitamins

See also A11 - *Vitamins*

B05XX Other i.v. solution additives

This group comprises all i.v. additives, which cannot be classified in the preceding groups.

B05Z HEMODIALYTICS AND HEMOFILTRATES

B05ZA Hemodialytics, concentrates

B05ZB Hemofiltrates

B06 OTHER HEMATOLOGICAL AGENTS

No DDDs are established in this group.

B06A OTHER HEMATOLOGICAL AGENTS

This group includes preparations for local and systemic use, and also some preparations used for dissolving clots in catheters, hemodialysis clots etc.

See also:

V07A - *All other non-therapeutic products*

B01AB - *Heparin group*

B06AA Enzymes

This group comprises enzymes with fibrinolytic properties. Enzymes with other well defined therapeutic use should be classified in the respective groups, see e.g.:

A09A - *Digestives, incl. enzymes*

B01AD - *Enzymes*

D03BA - *Proteolytic enzymes*

S01KX - *Other surgical aids*

B06AB Other hem products

C CARDIOVASCULAR SYSTEM

C01 CARDIAC THERAPY

- A Cardiac glycosides*
- B Antiarrhythmics, class I and III*
- C Cardiac stimulants excl. cardiac glycosides*
- D Vasodilators used in cardiac diseases*
- E Other cardiac preparations*

C02 ANTIHYPERTENSIVES

- A Antiadrenergic agents, centrally acting*
- B Antiadrenergic agents, ganglion-blocking*
- C Antiadrenergic agents, peripherally acting*
- D Arteriolar smooth muscle, agents acting on*
- K Other antihypertensives*
- L Antihypertensives and diuretics in combination*
- N Combinations of antihypertensives in ATC-gr. C02*

C03 DIURETICS

- A Low-ceiling diuretics, thiazides*
- B Low-ceiling diuretics, excl. thiazides*
- C High-ceiling diuretics*
- D Potassium-sparing agents*
- E Diuretics and potassium-sparing agents in combination*
- X Other diuretics*

C04 PERIPHERAL VASODILATORS

- A Peripheral vasodilators*

C05 VASOPROTECTIVES

- A Agents for treatment of hemorrhoids and anal fissures for topical use*
- B Antivaricose therapy*
- C Capillary stabilizing agents*

C07 BETA BLOCKING AGENTS

- A Beta blocking agents*
- B Beta blocking agents and thiazides*
- C Beta blocking agents and other diuretics*
- D Beta blocking agents, thiazides and other diuretics*
- E Beta blocking agents and vasodilators*
- F Beta blocking agents and other antihypertensives*

- C08** **CALCIUM CHANNEL BLOCKERS**
C Selective calcium channel blockers with mainly vascular effects
D Selective calcium channel blockers with direct cardiac effects
E Non-selective calcium channel blockers
G Calcium channel blockers and diuretics
- C09** **AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM**
A ACE inhibitors, plain
B ACE inhibitors, combinations
C Angiotensin II antagonists, plain
D Angiotensin II antagonists, combinations
X Other agents acting on the renin-angiotensin system
- C10** **LIPID MODIFYING AGENTS**
A Lipid modifying agents, plain
B Lipid modifying agents, combinations

C CARDIOVASCULAR SYSTEM

C01 CARDIAC THERAPY

C01A CARDIAC GLYCOSIDES

This group comprises plain and combined preparations containing cardiac glycosides, incl. standardized herbal extracts. Cardiac glycosides in combination with substances in group C01D and C01E are classified in this group. Combinations with antihypertensives, beta blocking agents, calcium channel blockers and ACE inhibitors, see group C02, C07, C08 and C09 respectively.

The DDDs are based on the average maintenance dose for the treatment of cardiac failure. Exception: the DDD for deslanoside is for acute treatment.

C01AA Digitalis glycosides

Combinations with diuretics are classified here.

C01AB Scilla glycosides

C01AC Strophantus glycosides

C01AX Other cardiac glycosides

This group includes e.g. peruvoside convallaria glycosides.

C01B ANTIARRHYTHMICS, CLASS I AND III

This group comprises preparations used in the treatment of arrhythmias.

The agents are listed according to the Vaughan Williams classification of antiarrhythmics. The division of class I antiarrhythmics may vary, depending on the literature used. The 3rd ed. of Avery's "Drug Treatment" (1987) and "Drugs" 31, 93 - 95, 1986 are used as a basis for the ATC classification. Class II antiarrhythmics see C07 and class IV, see C08 (e.g. verapamil).

Adenosine, which is also used as an antiarrhythmic, is classified in C01EB.

Combined preparations are classified at separate 5th levels using the corresponding 50-series. Combinations with psycholeptics are classified at separate 5th levels using the corresponding 70-series. Combinations with an antihypertensive e.g. reserpine are classified in C02AA.

The DDDs are based on the prophylaxis and treatment of supraventricular and ventricular arrhythmias. The DDDs are based on the maintenance dose. Preparations for parenteral administration are only used initially and are therefore given the same DDD as oral preparations.

C01BA Antiarrhythmics, class Ia

Combinations containing quinidine and verapamil are classified in C08DA.

C01BB Antiarrhythmics, class Ib

Lidocaine used as a local anaesthetic is classified in N01BB. Phenytoin, a class Ib antiarrhythmic, is classified as an antiepileptic in N03.

C01BC Antiarrhythmics, class Ic

C01BD Antiarrhythmics, class III

Sotalol, which has class III antiarrhythmic properties, is classified in C07AA.

The DDD for ibutilide refer to ibutilide fumarate.

C01BG Other antiarrhythmics, class I and III

C01C CARDIAC STIMULANTS EXCL. CARDIAC GLYCOSIDES

This group comprises agents for the treatment of hypotension. Respiratory stimulants are classified in R07AB.

Dihydroergotamine, which is used in the treatment of migraine as well as hypotension, is classified in N02CA - *Ergot alkaloids*.

Combinations with peripheral vasodilators, see C04 - *Peripheral vasodilators*.

This group includes various drugs used on different indications. The DDDs are therefore established individually for each substance (i.e. each ATC 5th level).

C01CA *Adrenergic and dopaminergic agents*

This group comprises sympathomimetics used in the treatment of hypotension. Etilefrin in combination with dihydroergotamine is classified in this group. Oral products of ephedrine are classified in R03CA.

C01CE *Phosphodiesterase inhibitors*

Phosphodiesterase inhibitors such as theophylline, which are used in asthma therapy, are classified in R03D.

C01CX *Other cardiac stimulants*

This group includes agents, which cannot be classified in the preceding groups.

C01D VASODILATORS USED IN CARDIAC DISEASES

This group comprises preparations used in ischemic heart diseases. See also C02 - *Antihypertensives*, C03 - *Diuretics*, C04 - *Peripheral vasodilators*, C07 - *Beta blocking agents*, C08 - *Calcium channel blockers* and C09 - *Agents acting on the renin-angiotensin system*.

Combinations with cardiac glycosides, see C01A.

Combinations with rauwolfia alkaloids, see C02AA.

Combinations with beta blocking agents, see C07.

Combinations with calcium channel blockers, see C08.

C01DA Organic nitrates

This group comprises nitrates used on the indication angina pectoris, including transdermal preparations. Amyl nitrite is classified in V03AB - *Antidotes*.

Combinations of isosorbide dinitrate and hydralazine are classified in C01DA58.

All nitrate preparations in combination with psycholeptics are classified in C01DA70. Nitrates in combination with psycholeptics and other agents are also given the code C01DA70.

The DDDs for the nitrates are mainly based on the treatment of angina pectoris attacks (3-4 times daily). The DDDs of preparations for oral and transdermal administration are higher than the DDDs for other routes of administration (e.g. sublingual) due to a lower bioavailability.

The DDDs for some preparations are mainly based on prophylaxis, for instance the DDDs of isosorbide dinitrate and glyceryl trinitrate plaster.

No DDDs are established for parenteral preparations due to great differences in the dosages used.

C01DB Quinolone vasodilators

C01DX Other vasodilators used in cardiac diseases

This group comprises vasodilators used in cardiac diseases, which cannot be classified in the preceding groups.

C01E OTHER CARDIAC PREPARATIONS

This group comprises various preparations used in the treatment of ischemic heart diseases, which cannot be classified in any of the preceding groups.

C01EA *Prostaglandins*

This group comprises e.g. alprostadil. Specific formulations of alprostadil for treatment of erectile dysfunction are classified in G04BE01.

The DDD for alprostadil equals the content of active substance in one ampoule.

C01EB *Other cardiac preparations*

This group comprises plain products used in the treatment of ischemic heart diseases, which cannot be classified in the preceding groups.

Adenosine, which is also used as an antiarrhythmic, is classified here. Antiarrhythmics, see C01B.

Other cardiovascular agents which cannot be classified in ATC group C02-C09 are also classified here.

Products containing indometacin or ibuprofen, which are only used for closing the ductus arteriosus in premature infants, are classified here. Indometacin used as an antiinflammatory agent is classified in M01AB01 or S01BC01.

The DDD for ibuprofen is based on the course dose.

C01EX *Other cardiac combination products*

This group comprises combined preparations, which cannot be classified in the preceding groups.

C02 ANTIHYPERTENSIVES

See also C03 - *Diuretics*, C07 - *Beta blocking agents*, C08 - *Calcium channel blockers* and C09 - *Agents acting on the renin-angiotensin system*.

Antihypertensives are mainly classified at 3rd levels according to the mechanism of action. Most headings are self-explanatory:

- C02A *Antiadrenergic agents, centrally acting*
- C02B *Antiadrenergic agents, ganglion-blocking*
- C02C *Antiadrenergic agents, peripherally acting*
- C02D *Arteriolar smooth muscle, agents acting on*
- C02K *Other antihypertensives*
- C02L *Antihypertensives and diuretics in combination*
- C02N *Combinations of antihypertensives in ATC gr. C02*

The oral DDDs are based on the average doses needed to reduce the blood pressure to a normal level in patients with mild-moderate hypertension.

Parenteral DDDs are based on dosages used for the treatment of hypertensive crises and are based on the content of the active ingredient pr. vial (ampoule).

C02A ANTIADRENERGIC AGENTS, CENTRALLY ACTING

C02AA *Rauwolfia alkaloids*

This group comprises plain and combined rauwolfia preparations used in hypertension.

There are separate 5th levels for combinations of rauwolfia alkaloids (C02AA03) and for rauwolfia, whole root (C02AA04).

Combinations with beta blocking agents, see C07F - *Beta blocking agents and other antihypertensives*.

Combinations with diuretics, see C02LA - *Rauwolfia alkaloids and diuretics in combination*.

Combinations with other antihypertensives, see C02N - *Combinations of antihypertensives*.

Combined products are otherwise classified at separate 5th levels using the corresponding 50-series.

C02AB *Methyldopa*

Combinations with diuretics, see C02LB - *Methyldopa and diuretics in combination*.

Combinations with Rauwolfia alkaloids and diuretics, see C02LA - *Rauwolfia alkaloids and diuretics in combination*.

Different DDDs have been established for the various stereoisomeric forms of methyldopa, because of different potency.

C02AC *Imidazoline receptor agonists*

Low strength clonidine preparations used in the treatment of migraine are classified in N02C - *Antimigraine preparations*.

Combinations with diuretics, see C02LC - *Imidazoline receptor agonists in combination with diuretics*.

C02B ANTIADRENERGIC AGENTS, GANGLION-BLOCKING

C02BA *Sulfonium derivatives*

C02BB *Secondary and tertiary amines*

C02BC *Bisquaternary ammonium compounds*

C02C ANTIADRENERGIC AGENTS, PERIPHERALLY ACTING

Alpha- and beta-blocking agents, see C07AG.

C02CA Alpha-adrenoreceptor antagonists

Combinations with diuretics, see C02LE - *Alpha-adrenoreceptor antagonists and diuretics*.

Alfuzosin and terazosin are classified in G04CA.

C02CC Guanidine derivatives

Combinations with diuretics, see C02LF - *Guanidine derivatives and diuretics*.

C02D ARTERIOLAR SMOOTH MUSCLE, AGENTS ACTING ON

See also C08 - *Calcium channel blockers*.

C02DA Thiazide derivatives

Parenteral preparations of diazoxide are classified here.

Oral preparations containing diazoxide for treatment of hypoglycemia are classified in V03AH.

C02DB Hydrazinophthalazine derivatives

Combinations with diuretics, see C02LG - *Hydrazinophthalazine derivatives and diuretics*.

Combinations of isosorbide dinitrate and hydralazine are classified in C01DA - *Organic nitrates*.

The oral DDD of dihydralazine is higher than the parenteral DDD. The parenteral DDD is given as the chloride salt while the oral DDD is given as the mesylate salt.

C02DC Pyrimidine derivatives

Minoxidil for systemic use is classified here.

Dermatological preparations containing minoxidil are classified in D11AX.

C02DD *Nitroferricyanide derivatives*

C02DG *Guanidine derivatives*

C02K OTHER ANTIHYPERTENSIVES

This group comprises all antihypertensives which cannot be classified in groups C02A-D, C02L, C02N, C03 - *Diuretics*, C07 - *Beta blocking agents*, C08 - *Calcium channel blockers* or C09 - *Agents acting on the renin-angiotensin system*.

C02KA *Alkaloids, excl. rauwolfia*

C02KB *Tyrosine hydroxylase inhibitors*

C02KC *MAO inhibitors*

C02KD *Serotonin antagonists*

C02KX *Other antihypertensives*

Sildenafil is classified in G04BE, even though some products are used for treatment of pulmonary arterial hypertension.

The DDDs are based on treatment of pulmonary arterial hypertension.

C02L ANTIHYPERTENSIVES AND DIURETICS IN COMBINATION

All substances classified in groups C02A-K, in combination with diuretics are classified in this group. At each 5th level, various combinations containing e.g. different diuretics, other antihypertensives or potassium may occur.

Combinations with beta blocking agents, see comments under C07.

Diuretics in combination with calcium channel blockers are classified in C08.

Diuretics in combination with ACE inhibitors, are classified in C09BA.

Diuretics in combination with angiotensin II antagonists are classified in C09DA.

The need for a systematic approach to classify combinations of different antihypertensives has resulted in a ranking according to the ATC codes. Substances classified in ATC group C02AA take precedence over C02AB and substances in C02A take precedence over C02B etc.

Example: A combined preparation containing bietaserpine, hydralazine and hydrochlorothiazide will be given the code C02LA07 according to the above mentioned ranking.

Combinations with psycholeptics are classified at separate 5th levels using the corresponding 70-series.

It has been considered most appropriate to assign fixed DDDs based on the average use of the different combinations without considering and comparing the strengths of the various components. 1 tablet is the fixed DDD for products given once daily whereas the fixed DDD for products given twice daily and three times daily is respectively 2 tablets and 3 tablets. The assigned DDDs cannot always be compared with the DDDs assigned for plain preparations.

- C02LA Rauwolfia alkaloids and diuretics in combination*
- C02LB Methyldopa and diuretics in combination*
- C02LC Imidazoline receptor agonists in combination with diuretics*
- C02LE Alpha-adrenoreceptor antagonists and diuretics*
- C02LF Guanidine derivatives and diuretics*
- C02LG Hydrazinophthalazine derivatives and diuretics*
- C02LK Alkaloids, excl. rauwolfia, in combination with diuretics*
- C02LL MAO inhibitors and diuretics*
- C02LN Serotonin antagonists and diuretics*

C02LX Other antihypertensives and diuretics

C02N COMBINATIONS OF ANTIHYPERTENSIVES IN ATC-GR. C02

Comprises combinations of different antihypertensives classified in ATC-gr. C02.

Antihypertensives in combination with diuretics are classified in C02L - *Antihypertensives and diuretics in combination*.

Combinations with beta blocking agents, see C07F - *Beta blocking agents and other antihypertensives*.

The DDDs for fixed combinations are commented in C02L.

C03 **DIURETICS**

This group comprises diuretics, plain and in combination with potassium or other agents. Vasopressin antagonists are also included in this group. Potassium-sparing agents are classified in C03D and C03E.

Combinations with digitalis glycosides, see C01AA.

Combinations with antihypertensives, see C02L - *Antihypertensives and diuretics in combination*.

Combinations with beta blocking agents, see C07B - C07D.

Combinations with calcium channel blockers, see C08.

Combinations with agents acting on the renin angiotensin system, see C09B and C09D.

The DDDs for diuretics are based on monotherapy. Most diuretics are used both for the treatment of edema and hypertension in similar doses and the DDDs are therefore based on both indications.

The DDDs for combinations correspond to the DDD for the diuretic component, except for ATC group C03E, see comments under this level.

C03A LOW-CEILING DIURETICS, THIAZIDES

Combinations with potassium-sparing agents, see C03EA.

The different lipid solubility of the thiazides should be considered when assigning DDDs.

C03AA Thiazides, plain

C03AB Thiazides and potassium in combination

The 5th levels correspond to those in C03AA:

C03AA01 - bendroflumethiazide

C03AB01 - bendroflumethiazide and potassium

C03AH Thiazides, combinations with psycholeptics and/or analgesics

C03AX Thiazides, combinations with other drugs

C03B LOW-CEILING DIURETICS, EXCL. THIAZIDES

This group comprises all low-ceiling diuretics not classified in C03A.

Combinations with potassium-sparing agents, see C03EA.

C03BA Sulfonamides, plain

C03BB Sulfonamides and potassium in combination

The 5th levels correspond to those in C03BA, see example in C03AB.

C03BC Mercurial diuretics

C03BD Xanthine derivatives

Includes e.g. theobromine. See also R03DA - *Xanthines*.

C03BK Sulfonamides, combinations with other drugs

Includes e.g. combination with psycholeptics.

C03BX Other low-ceiling diuretics

All low-ceiling diuretics which cannot be classified in the preceding groups are classified here.

C03C HIGH-CEILING DIURETICS

This group comprises high-ceiling diuretics (loop-diuretics) e.g. furosemide.

Combinations with potassium-sparing agents, see C03EB.

C03CA Sulfonamides, plain

C03CB Sulfonamides and potassium in combination

The 5th levels correspond to those in C03CA. See example in C03AB.

C03CC Aryloxyacetic acid derivatives

C03CD Pyrazolone derivatives

C03CX Other high-ceiling diuretics

All high-ceiling diuretics which cannot be classified in the preceding groups are classified here.

C03D POTASSIUM-SPARING AGENTS

C03DA Aldosterone antagonists

C03DB Other potassium-sparing agents

C03E **DIURETICS AND POTASSIUM-SPARING AGENTS IN COMBINATION**

Fixed DDDs are assigned for combinations in this group. E.g. 1 tablet regardless of strengths is the DDD assigned for hydrochlorothiazide and amiloride in combinations. See comments to C02L also.

C03EA *Low-ceiling diuretics and potassium-sparing agents*

C03EB *High-ceiling diuretics and potassium-sparing agents*

C03X **OTHER DIURETICS**

C03XA *Vasopressin antagonists*

C04 **PERIPHERAL VASODILATORS**

C04A **PERIPHERAL VASODILATORS**

This group comprises plain and combined preparations used in the treatment of cerebrovascular or peripheral circulatory disorders.

Combinations with Antihypertensives, see C02 - *Antihypertensives*.

Combinations with vasodilators used in cardiac diseases, see C01DA.

The DDDs are based on the doses used for the treatment of cerebral and peripheral vascular disorders.

C04AA *2-amino-1-phenylethanol derivatives*

C04AB *Imidazoline derivatives*

The DDD for phentolamine is based on the treatment of acute heart failure and is based on parenteral use.

C04AC Nicotinic acid and derivatives

Includes low strength preparations (e.g. nicotinic acid tablets 50 mg). Nicotinic acid preparations in high strength (e.g. nicotinic acid tablets 500 mg) is used as a cholesterol reducer and is classified in C10AD.

C04AD Purine derivatives

Combinations with nicotinic acid and derivatives are allowed at each 5th level.

C04AE Ergot alkaloids

Includes combinations with other peripheral vasodilators.

Combinations with calcium channel blockers are classified in C08CA.

See also G02AB and N02CA.

C04AF Enzymes

C04AX Other peripheral vasodilators

Betahistine, cinnarizine and flunarizine are classified as antivertigo preparations in N07CA.

Papaverine preparations, see A03AD and G04BE.

C05 VASOPROTECTIVES

No DDDs are established in this group, since most of the drugs in this group are for topical use.

C05A AGENTS FOR TREATMENT OF HEMORRHOIDS AND ANAL FISSURES FOR TOPICAL USE

This group comprises agents for local use, such as suppositories, ointments etc. Preparations used for treatment of perineal trauma are classified here.

C05AA Corticosteroids

All antihemorrhoidal products, which contain corticosteroids, are classified in this group, including both plain products and combinations with antiinfectives, local anesthetics etc. At each 5th plain level, combinations may occur.

C05AB Antibiotics

All antihemorrhoidal products which contain antibiotics, excl. combinations with corticosteroids, are classified in this group. At each 5th level combinations may occur.

C05AD Local anesthetics

All antihemorrhoidal products which contain anesthetics, excl. combinations with corticosteroids and/or antibiotics, are classified in this group. At each 5th plain level, combinations may occur.

See also D04AB - *Anesthetics for topical use* and N01B - *Local anesthetics*.

C05AE Muscle relaxants

Topical products containing glyceryl trinitrate or isosorbide dinitrate are classified in this group.

C05AX Other agents for treatment of hemorrhoids and anal fissures for topical use

Agents which cannot be classified in the preceding groups are classified in this group, e.g. bismuth/zinc oxide-preparations.

C05B ANTIVARICOSE THERAPY

This group comprises all products for treatment of varices, i.v. infusion induced thrombophlebitis etc.

Zinc bandages, see D09A - *Medicated dressings*.

C05BA Heparins or heparinoids for topical use

Heparin in combination with e.g. dexpanthenol and allantoin is classified in C05BA53.

Heparin in combination with diclofenac for topical use is classified in M02AA15.

Heparinoids in combination with calcium dobesilate are classified in C05BX - *Other sclerosing agents*.

C05BB Sclerosing agents for local injection

C05BX Other sclerosing agents

Combinations of calcium dobesilate and heparinoids are classified here.

C05C CAPILLARY STABILIZING AGENTS

C05CA Bioflavonoids

Rutoside is classified in this group.
Oxerutines are classified in C05CA54.

Combinations with other capillary stabilizing agents are classified at separate 5th levels using the corresponding 50-series.

C05CX Other capillary stabilizing agents

C07 BETA BLOCKING AGENTS

C07A BETA BLOCKING AGENTS

All plain beta blocking agents are classified in this group. Combination packages containing two different products (e.g. sotalol tablets and aspirin tablets in a combination package) are also classified in this group.

Labetalol, and carvedilol are classified in C07AG - *Alpha- and beta blocking agents*.

The DDDs are based on the treatment of mild-moderate hypertension.

The DDDs for oral and parenteral formulations are equal, even if the parenteral preparations are used for the initial treatment of arrhythmias. Exception: practolol.

C07AA Beta blocking agents, non-selective

All plain non-selective beta blocking agents are classified in this group. Combined packages containing sotalol tablets and aspirin tablets are classified in C07AA57.

C07AB Beta blocking agents, selective

All plain selective beta blocking agents are classified in this group.

The s-enantiomer and the racemate of atenolol are classified at separate 5th levels.

Different DDDs have been assigned for the two stereoisomeric forms of atenolol due to different potency.

C07AG Alpha and beta blocking agents

C07B BETA BLOCKING AGENTS AND THIAZIDES

This group comprises combinations of beta blocking agents and thiazides. Different thiazides may occur at each 5th level.

Combinations of beta blocking agents, thiazides and other agents are classified at separate 5th levels using the 50-series.

See comments to C02L concerning the principles for assignment of DDDs for the combined preparations.

C07BA Beta blocking agents, non-selective, and thiazides

C07BB Beta blocking agents, selective, and thiazides

C07BG Alpha and beta blocking agents and thiazides

C07C BETA BLOCKING AGENTS AND OTHER DIURETICS

This group comprises combinations of beta blocking agents and diuretics excl. thiazides. Different diuretics except thiazides, may occur at each 5th level.

Combinations with other agents in addition, are classified at separate 5th levels using the 50-series.

See comments to C02L concerning the principles for assignment of DDDs for combined preparations.

C07CA Beta blocking agents, non-selective, and other diuretics

C07CB Beta blocking agents, selective, and other diuretics

C07CG Alpha and beta blocking agents and other diuretics

C07D BETA BLOCKING AGENTS, THIAZIDES AND OTHER DIURETICS

This group comprises combinations of beta blocking agents, thiazides and other diuretics. Different thiazides and diuretics may occur at each 5th level.

Combinations with other agents in addition, are classified at separate 5th levels using the 50-series.

See comments to C02L concerning the principles for assignment of DDDs for combined preparations.

C07DA Beta blocking agents, non-selective, thiazides and other diuretics

C07DB Beta blocking agents, selective, thiazides and other diuretics

C07E BETA BLOCKING AGENTS AND VASODILATORS

This group comprises beta blocking agents and vasodilators (excl. calcium channel blockers) in combination.

Combinations with calcium channel blockers are classified in C07F.

See comments to C02L concerning the principles for assignment of DDDs for combined preparations.

C07EA Beta blocking agents, non-selective, and vasodilators

C07EB Beta blocking agents, selective, and vasodilators

C07F BETA BLOCKING AGENTS AND OTHER ANTIHYPERTENSIVES

This group comprises combinations of beta blocking agents and antihypertensives. Different antihypertensives may occur at each 5th level.

Beta blocking agents in combination with calcium channel blockers are classified in this group.

See comments to C02L concerning the principles for assignment of DDDs for combined preparations.

C07FA Beta blocking agents, non-selective, and other antihypertensives

C07FB Beta blocking agents, selective, and other antihypertensives

C08 CALCIUM CHANNEL BLOCKERS

The calcium channel blockers are classified according to selectivity of calcium channel activity and direct cardiac effects. The ATC 4th levels are subdivided according to chemical structure.

Combinations with ergot alkaloids (C04AE) are classified in this group by using the 50-series.

Combinations with diuretics are classified in C08G.

Combinations with ACE inhibitors are classified in C09BB.

Combinations with beta blocking agents are classified in C07F.

The DDDs for calcium channel blockers are based on the treatment of mild-moderate hypertension, although some are used for other indications (e.g. angina pectoris).

The DDDs for oral and parenteral preparations are equal and are based on the oral dose, since oral preparations represent the major fraction of the total consumption.

C08C SELECTIVE CALCIUM CHANNEL BLOCKERS WITH MAINLY VASCULAR EFFECTS

C08CA Dihydropyridine derivatives

Preparations containing nifedipine in combination with ergot alkaloids are classified in C08CA55.

Combinations with diuretics are classified in C08G.

Amlodipine in combination with atorvastatin is classified in C10BX03.

C08CX Other selective calcium channel blockers with mainly vascular effects

C08D SELECTIVE CALCIUM CHANNEL BLOCKERS WITH DIRECT CARDIAC EFFECTS

C08DA Phenylalkylamine derivatives

Combinations containing verapamil and quinidine are classified in C08DA51.

C08DB Benzothiazepine derivatives

C08E NON-SELECTIVE CALCIUM CHANNEL BLOCKERS

C08EA *Phenylalkylamine derivatives*

C08EX *Other non-selective calcium channel blockers*

C08G CALCIUM CHANNEL BLOCKERS AND DIURETICS

C08GA *Calcium channel blockers and diuretics*

C09 AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM

The DDDs are based on the treatment of mild-moderate hypertension.

See comments to C02L concerning the principles for assignment of DDDs for combined preparations.

C09A ACE INHIBITORS, PLAIN

All plain ACE inhibitors are classified in this group. No separate ATC codes are assigned for the esters of the ACE inhibitors (e.g. enalaprilat, quinaprilat).

Combinations with diuretics, see C09BA - *ACE inhibitors and diuretics*.

Combinations with calcium channel blockers, see C09BB - *ACE inhibitors and calcium channel blockers*.

C09AA *ACE inhibitors, plain*

C09B ACE INHIBITORS, COMBINATIONS

Combinations of ramipril, simvastatin, and acetylsalicylic acid are classified in C10BX.

C09BA *ACE inhibitors and diuretics*

C09BB ACE inhibitors and calcium channel blockers

C09C ANGIOTENSIN II ANTAGONISTS, PLAIN

C09CA Angiotensin II antagonists, plain

C09D ANGIOTENSIN II ANTAGONISTS, COMBINATIONS

C09DA Angiotensin II antagonists and diuretics

C09DB Angiotensin II antagonists and calcium channel blockers

Combinations with hydrochlorothiazide are classified in C09DX.

C09DX Angiotensin II antagonists, other combinations

C09X OTHER AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM

C09XA Renin-inhibitors

Fixed combinations of aliskiren and valsartan are classified in C09DX.

C10 LIPID MODIFYING AGENTS

The DDDs are based on the treatment of hypercholesterolemia.

C10A LIPID MODIFYING AGENTS, PLAIN

Combinations of different cholesterol and triglyceride reducers are classified at separate 5th levels using the corresponding 50-series. The following ranking according to the ATC codes is used: Substances classified in ATC-group C10AA take precedence over C10AB etc.

Pantethine, which is also used in the treatment of hyperlipidemi, is classified as a vitamin in A11HA.

C10AA HMG CoA reductase inhibitors

This group comprises agents which act as competitive inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMG CoA reductase).

Atorvastatin in combination with amlodipine is classified in C10BX03.

C10AB Fibrates

Clofibrate and analogues are classified here.

The DDD for fenofibrate is based on the micronised formulation.

C10AC Bile acid sequestrants

This group comprises substances (such as colestyramine and colestipol) which reduces the cholesterol level by increasing the excretion of bile acid.

C10AD Nicotinic acid and derivatives

This group comprises high strength preparations (e.g. nicotinic acid tab 500 mg) used as cholesterol reducers. Nicotinic acid or derivatives in low strength preparations (e.g. nicotinic acid tab 50 mg) are classified in C04A - *Peripheral vasodilators*.

Combinations of nicotinic acid and laropiprant are classified in C10AD52.

C10AX Other lipid modifying agents

This group comprises all cholesterol and triglyceride reducers, which cannot be classified in the preceding groups.

Sulodexide is classified in B01AB.

C10B LIPID MODIFYING AGENTS, COMBINATIONS

C10BA HMG CoA reductase inhibitors in combination with other lipid modifying agents

The DDD for the fixed combination of simvastatin and ezetimibe is 1 UD (1 tablet), regardless of strength.

C10BX HMG CoA reductase inhibitors, other combinations

D DERMATOLOGICALS

D01 ANTIFUNGALS FOR DERMATOLOGICAL USE

- A Antifungals for topical use*
- B Antifungals for systemic use*

D02 EMOLLIENTS AND PROTECTIVES

- A Emollients and protectives*
- B Protectives against UV-radiation*

D03 PREPARATIONS FOR TREATMENT OF WOUNDS AND ULCERS

- A Cicatrizants*
- B Enzymes*

D04 ANTIPRURITICS, INCL. ANTIHISTAMINES, ANESTHETICS, ETC.

- A Antipruritics, incl. antihistamines, anesthetics, etc.*

D05 ANTIPSORIATICS

- A Antipsoriatics for topical use*
- B Antipsoriatics for systemic use*

D06 ANTIBIOTICS AND CHEMOTHERAPEUTICS FOR DERMATOLOGICAL USE

- A Antibiotics for topical use*
- B Chemotherapeutics for topical use*
- C Antibiotics and chemotherapeutics, combinations*

D07 CORTICOSTEROIDS, DERMATOLOGICAL PREPARATIONS

- A Corticosteroids, plain*
- B Corticosteroids, combinations with antiseptics*
- C Corticosteroids, combinations with antibiotics*
- X Corticosteroids, other combinations*

D08 ANTISEPTICS AND DISINFECTANTS

- A Antiseptics and disinfectants*

D09 MEDICATED DRESSINGS

- A Medicated dressings*

D10 **ANTI-ACNE PREPARATIONS**

A *Anti-acne preparations for topical use*

B *Anti-acne preparations for systemic use*

D11 **OTHER DERMATOLOGICAL PREPARATIONS**

A *Other dermatological preparations*

D **DERMATOLOGICALS**

Most of the drugs in this group are preparations for topical use. Some few preparations for systemic use with clear dermatological applications, e.g. griseofulvin (antimycotic), retinoids (for treatment of acne) and psoralens and retinoids (for treatment of psoriasis) are classified in this group.

Only oral preparations in ATC group D are given DDDs. Most products in this group are for topical use, and no DDDs are assigned because the amount given per day can vary very much according to the intensity and distribution of the disease. Consumption figures for these dermatological preparations can be expressed in grams of preparations regardless of strength.

D01 ANTIFUNGALS FOR DERMATOLOGICAL USE

This group comprises preparations for topical and systemic treatment of dermatological mycoses. Preparations with systemic antimycotic effect, see also J02A - *Antimycotics for systemic use*.

Topical preparations used especially in gynecological infections are classified in G01A - *Antiinfectives and antiseptics, excl. combinations with corticosteroids* or G01B - *Antiinfectives/antiseptics in combination with corticosteroids*. Preparations for local treatment of fungal infections in the mouth, see A01AB - *Antiinfectives and antiseptics for local oral treatment*.

D01A ANTIFUNGALS FOR TOPICAL USE

Combined preparations are classified in this group if mycosis is the main indication.

D01AA Antibiotics

Preparations used in the treatment of bacterial dermatological infections, see D06A - *Antibiotics for topical use*.

D01AC Imidazole and triazole derivatives

Shampoos containing imidazoles are classified here. Topical metronidazole is mainly used in rosacea and is classified in D06BX - *Other chemotherapeutics*.

Combinations with corticosteroids are classified in D01AC20. All other combinations are classified by using the 50-series e.g. miconazole and zinc.

Combinations of clotrimazole, gentamicin and corticosteroids are classified in D07C.

D01AE Other antifungals for topical use

See also D08AH - *Quinoline derivatives*

Combined preparations containing salicylic acid, which are used as antifungals (e.g. dusting powders), are classified in this group in D01AE20. See also D02AF - *Salicylic acid preparations*.

Derivatives of undecylenic acid are classified in D01AE04.

D01B ANTIFUNGALS FOR SYSTEMIC USE

This group comprises preparations used in the systemic treatment of dermatological mycoses. See also J02A - *Antimycotics for systemic use*.

D01BA Antifungals for systemic use

The DDDs for griseofulvin and terbinafine are based on the treatment of dermatophyte infections in skin, hair or nails.

D02 EMOLLIENTS AND PROTECTIVES

D02A EMOLLIENTS AND PROTECTIVES

This group comprises all types of emollients and protectives with no specific therapeutic effect or use, and also preparations for use in wounds, which are not classified in D09 - *Medicated dressings*.

Some similar products are classified in D03A - *Cicatrizants*, e.g. cod-liver oil ointments.

D02AA Silicone products

D02AB Zinc products

D02AC Soft paraffin and fat products

Some similar products with a higher water content (creams) are classified in D02AX - *Other emollients and protectives*. Soft paraffin dressings, see D09AX.

D02AD Liquid plasters

Liquid plasters are classified in this group whereas non-medicated adhesive plasters, surgical tapes etc. are classified in V07AA.

D02AE Carbamide products

D02AF Salicylic acid preparations

Preparations containing salicylic acid used for the treatment of mycosis are classified in D01AE - *Other antifungals for topical use*.

Salicylic acid in combination with corticosteroids, see D07X.

Medicated shampoos containing salicylic acid are classified in D11AC30 - *others*.

All other preparations containing salicylic acid, including anti-acne preparations, should be classified in this group.

D02AX Other emollients and protectives

Soft paraffin and fat products with high water content (creams) are classified in this group. See also D02AC - *Soft paraffin and fat products*.

Weak boric acid vaseline is classified here.

Other boric acid products are classified in D08AD.

D02B **PROTECTIVES AGAINST UV-RADIATION**

This group comprises special protectives against UV-radiation.

D02BA *Protectives against UV-radiation for topical use*

Derivatives may be included in each plain 5th level.

D02BB *Protectives against UV-radiation for systemic use*

The DDD of betacarotene is based on the treatment of patients with erythropoietic protoporphyria.

D03 **PREPARATIONS FOR TREATMENT OF WOUNDS AND ULCERS**

Topical preparations used in the treatment of wounds and ulcers, e.g. leg ulcers, are classified in this group. Protective ointments are classified in D02A - *Emollients and protectives*.

See also

D06 - *Antibiotic and chemotherapeutics for dermatological use*.

D08 - *Antiseptics and disinfectants*.

D09 - *Medicated dressings*.

D03A **CICATRIZANTS**

Topical vitamin preparations etc. are classified in this group if they cannot be classified in other groups.

D03AA *Cod-liver oil ointments*

D03AX *Other cicatrizants*

Includes e.g. dextranomer powders with or without antiseptics. See also D09A - *Medicated dressings*.

Medicated dressings containing hyaluronic acid are classified here.

Topical products containing glyceryl trinitrate or isosorbide dinitrate used for treatment of anal fissures are classified in C05AE.

D03B ENZYMES

Proteolytic enzymes for topical treatment of ulcers are classified here.

D03BA Proteolytic enzymes

D04 ANTIPRURITICS, INCL. ANTIHISTAMINES, ANESTHETICS, ETC.

D04A ANTIPRURITICS, INCL. ANTIHISTAMINES, ANESTHETICS, ETC.

This group comprises antipruritics for topical use in the treatment of pruritus, minor burns, insect stings, herpes zoster etc.

See also D07 - *Corticosteroids, dermatological preparations.*

D04AA Antihistamines for topical use

At each 5th level, antiseptics, siccants etc. may occur in combination with the antihistamines. Combinations with corticosteroids, see D07 - *Corticosteroids, dermatological preparations.*

Combinations with anesthetics are classified in D04AB.

Combinations of diphenhydramine and diethyltoluamid are classified at the plain level for diphenhydramine in D04AA.

D04AB Anesthetics for topical use

At each 5th plain level, antiseptics, siccants etc. may occur in combination with the anesthetics. Combinations with corticosteroids, see D07 - *Corticosteroids, dermatological preparations.*

Combinations with antihistamines are classified here.

See also C05A - *Agents for treatment of hemorrhoids and anal fissures for topical use*, and N01B - *Anesthetics, local.*

D04AX Other antipruritics

This group comprises ointments, creams, liniments etc. containing e.g. camphora, menthol, calamine. Crotonon is classified here. When classifying products in this group, alternative groups should be considered, e.g.:

D02 - *Emollients and protectives*

D08 - *Antiseptics and disinfectants*

M02 - *Topical products for joint and muscular pain*

D05 ANTIPSORIATICS

D05A ANTIPSORIATICS FOR TOPICAL USE

This group comprises products for topical use mainly for the treatment of psoriasis. Corticosteroids for topical use are classified in D07 - *Corticosteroids, dermatological preparations.*

D05AA Tars

All tar preparations for dermatological use are classified in this group, except for combinations with corticosteroids.

D05AC Antracen derivatives

D05AD Psoralens for topical use

D05AX Other antipsoriatics for topical use

Corticosteroids in combination with vitamin D analogues indicated only for the treatment of psoriasis are classified in D05AX.

D05B ANTIPSORIATICS FOR SYSTEMIC USE

This group comprises drugs for systemic use against psoriasis. Antineoplastic agents, sometimes used in severe psoriasis, are classified in group L - *Antineoplastic and immunomodulating agents.*

D05BA Psoralens for systemic use

The DDDs for psoralens for systemic use are based on the combined treatment with drug and UV-A irradiation.

D05BB Retinoids for treatment of psoriasis

Retinoids for the treatment of acne are classified in D10BA.

Alitretinoin used for hand eczema is classified in D11A.

D05BX Other antipsoriatics for systemic use

Alefacept and efalizumab are classified in L04AA.

D06 ANTIBIOTICS AND CHEMOTHERAPEUTICS FOR DERMATOLOGICAL USE

This group comprises products for topical use in skin infections etc.

D06A ANTIBIOTICS FOR TOPICAL USE

This group comprises antibiotics for dermatological use, except

Antibiotics with antimycotic properties - D01A

Combinations with chemotherapeutics - D06C

Combinations with corticosteroids - D07C

Antiinfectives for treatment of acne - D10AF

D06AA Tetracycline and derivatives

Combined preparations, which contain oxytetracycline and other antibiotics, are classified in D06AA03 - *oxytetracycline*.

D06AX Other antibiotics for topical use

Combined preparations, which contain neomycin and other antibiotics, are classified in D06AX04 - *neomycin*.

Combined preparations, which contain neomycin and bacitracin, are classified in D06AX04 – *neomycin*.

Combined preparations, containing bacitracin and other antibiotics, are classified in D06AX05 – *bacitracin*.

D06B CHEMOTHERAPEUTICS FOR TOPICAL USE

This group includes chemotherapeutics for dermatological use, except:

Combinations with antibiotics - D06C

Combinations with corticosteroids - D07C

D06BA Sulfonamides

D06BB Antivirals

Podophyllin preparations are classified at the 5th level for podophyllotoxin.

D06BX Other chemotherapeutics

This group comprises chemotherapeutics used in different skin disorders, which cannot be classified in the preceding groups, e.g. metronidazole for the treatment of rosacea.

D06C ANTIBIOTICS AND CHEMOTHERAPEUTICS, COMBINATIONS

D07 CORTICOSTEROIDS, DERMATOLOGICAL PREPARATIONS

As a main rule, all topical corticosteroid preparations should be classified in this group. There are, however, some few exceptions:

Combinations of corticosteroids and antiinfectives for gynaecological use, see G01B.

Corticosteroids for local oral treatment, see A01AC.

Anti-acne preparations, see D10A.

Antihemorrhoidals with corticosteroids, see C05AA.

Corticosteroids for ophthalmological or otological use, see S - *Sensory organs*.

D07A CORTICOSTEROIDS, PLAIN

The group is subdivided according to clinical potency of the steroids as such. Additional agents meant to enhance the penetration and increase the potency of the product do not influence the classification, neither do the strength of the preparations or the vehicle.

D07AA Corticosteroids, weak (group I)

D07AB Corticosteroids, moderately potent (group II)

D07AC Corticosteroids, potent (group III)

D07AD Corticosteroids, very potent (group IV)

D07B CORTICOSTEROIDS, COMBINATIONS WITH ANTISEPTICS

This group comprises combined corticosteroid/antiseptic preparations for dermatological use.

For most antifungal preparations with corticosteroids, the primary indication is mycosis and not inflammation. These products should be classified in D01A - *Antifungals for topical use*. Corticosteroids, antiseptics and salicylic acid in combination are classified in D07X.

The group is subdivided according to clinical potency, see D07A. Exceptions, see D07. At each 5th level various antiseptics may occur.

D07BA Corticosteroids, weak, combinations with antiseptics

D07BB Corticosteroids, moderately potent, combinations with antiseptics

D07BC Corticosteroids, potent, combinations with antiseptics

D07BD Corticosteroids, very potent, combinations with antiseptics

D07C CORTICOSTEROIDS, COMBINATIONS WITH ANTIBIOTICS

This group comprises combined corticosteroid/antibiotic preparations for dermatological use. The group is subdivided according to clinical potency, see D07A. Exceptions, see D07.

At each 5th level various antibiotics (incl. antifungals) may occur.

D07CA Corticosteroids, weak, combinations with antibiotics

D07CB Corticosteroids, moderately potent, combinations with antibiotics

D07CC Corticosteroids, potent, combinations with antibiotics

Combinations of beclomethasone, clotrimazole and gentamycin are classified here.

D07CD Corticosteroids, very potent, combinations with antibiotics

D07X CORTICOSTEROIDS, OTHER COMBINATIONS

This group comprises most other combined corticosteroid preparations for dermatological use, e.g. combinations with coal tar, carbamide and salicylic acid. Salicylic acid is regarded as a keratolytic agent. Preparations with salicylic acid and antiseptics are classified in this group, as salicylic acid is regarded as being more important than the antiseptics for the therapeutic use of these products (psoriasis, seborrhea).

The group is subdivided according to clinical potency, see D07A. Exceptions, see D07.

D07XA Corticosteroids, weak, other combinations

D07XB Corticosteroids, moderately potent, other combinations

D07XC Corticosteroids, potent, other combinations

D07XD Corticosteroids, very potent, other combinations

D08 ANTISEPTICS AND DISINFECTANTS

D08A ANTISEPTICS AND DISINFECTANTS

This group comprises all dermatological antiinfective preparations, which are not classified in any of the following groups:

D01 - *Antifungals for dermatological use*

D03A - *Cicatrizants*

D06 - *Antibiotics and chemotherapeutics for dermatological use*

D07B - *Corticosteroids, combinations with antiseptics*

D07X - *Corticosteroids, other combinations*

D09A - *Medicated dressings*

D10A - *Anti-acne preparations for topical use*

D11AC- *Medicated shampoos*

P03A - *Ectoparasitocides, incl. scabicides*

Antiviral agents, see D06BB.

Non-therapeutic auxiliary products, such as exploration creams and lubricants, are classified in V07AY. Lubricants, which contain antiseptics, are, however, classified in this group.

The group is subdivided according to chemical structure.

At each 5th plain level combinations with alcohols are allowed.

D08AA Acridine derivatives

D08AB Aluminium agents

Combinations with quarternary ammonium compounds are classified in D08AJ.

D08AC Biguanides and amidines

D08AD Boric acid products

Weak boric acid vaseline is classified in D02AX.

D08AE Phenol and derivatives

Each 5th level also allows combinations with alcohol.

D08AF Nitrofurran derivatives

D08AG Iodine products

See also D03AX and D09AA. Cadexomer iodine is classified in D03AX. Medicated dressings containing iodine are classified in D09AA.

D08AH Quinoline derivatives

Chloroquinaldol and clioquinol are classified in this group and not in D01 - *Antifungals for dermatological use*.

Chloroquinaldol and clioquinol for systemic use are classified in P01AA - *Hydroxyquinoline derivatives*

D08AJ Quaternary ammonium compounds

Combinations with aluminium agents are classified here.

D08AK Mercurial products

Combined products, which also contain silver compounds, are classified in this group.

D08AL Silver compounds

Combined products, which also contain mercury compounds, see D08AK.

D08AX Other antiseptics and disinfectants

D09 MEDICATED DRESSINGS

D09A MEDICATED DRESSINGS

This group comprises medicated dressings, ointment dressings etc. Liquid wound protectives are classified in D02AD - *Liquid plasters*. Local hemostatics, e.g. gauze, tampons etc. are classified in B02BC - *Local hemostatics*. Medicated dressings containing hyaluronic acid are classified in D03AX - *Other cicatrizants*.

D09AA Medicated dressings with antiinfectives

See also D03AX and D08AG. Products containing cadexomer iodine are classified in D03AX.

D09AB Zinc bandages

Zinc bandages with or without supplements are classified in this group.

D09AX Soft paraffin dressings

Dressings with antiinfectives, see D09AA.

Dressings with scarlet red are classified in this group.

D10 ANTI-ACNE PREPARATIONS

The DDDs are based on the treatment of severe acne.

D10A ANTI-ACNE PREPARATIONS FOR TOPICAL USE

This group comprises all topical preparations used specifically in the treatment of acne, incl. preparations with antibiotics, corticosteroids etc.

D10AA Corticosteroids, combinations for treatment of acne

Only combined corticosteroid preparations specifically used in the treatment of acne are classified in this group. Other dermatological corticosteroid preparations are classified in D07 - *Corticosteroids, dermatological preparations*.

D10AB Preparations containing sulfur

Preparations, which contain sulfur in addition to a sulfur derivative, should be classified at the 5th level of the derivative.

The products may contain other active ingredients such as resorcinol.

D10AD Retinoids for topical use in acne

All retinoids for topical use should be classified in D10AD.

D10AE Peroxides

Combinations with antiinfectives are classified in D10AF.

D10AF Antiinfectives for treatment of acne

This group comprises antibiotics for topical use with acne as the main indication.

Other topical antiinfectives are classified in D06 - *Antibiotics and chemotherapeutics for dermatological use*.

D10AX Other anti-acne preparations for topical use

D10B ANTI-ACNE PREPARATIONS FOR SYSTEMIC USE

This group comprises drugs for systemic use in the treatment of acne. Antibiotics, such as tetracyclines and erythromycin, which are also used for the treatment of acne, are classified in group J.

Combinations of e.g. estrogen and antiandrogen, used for the treatment of acne, are classified in group G03 - *Sex hormones and modulators of the genital system*.

D10BA Retinoids for treatment of acne

Retinoids used in severe psoriasis are classified in D05BB, whereas alitretinoin used for hand eczema is classified in D11A.

D10BX Other anti-acne preparations for systemic use

Ichtasol preparations for systemic use in treatment of acne are classified in this group.

D11 OTHER DERMATOLOGICAL PREPARATIONS

D11A OTHER DERMATOLOGICAL PREPARATIONS

This group comprises various dermatological preparations, which cannot be classified in the preceding groups.

Insect repellents are classified in P03B - *Insecticides and repellents*.

D11AA Antihidrotics

D11AC Medicated shampoos

Shampoos containing imidazoles are classified in D01AC.

Shampoos containing coal tar are classified in D05AA.

D11AE Androgens for topical use

D11AF Wart and anti-corn preparations

Preparations such as keratolytics for the treatment of common warts and cornified lesions are classified in this group.

Podophyllotoxin/podophyllin e.g. for the treatment of genital warts, is classified in D06BB.

D11AH Agents for atopic dermatitis, excluding corticosteroides

Corticosteroides used for atopic dermatitis, see D07.

D11AX Other dermatologicals

This group comprises products, which cannot be classified in the preceding groups. E.g. minoxidil for the treatment of male pattern baldness is classified here.

Lithium succinate in combination with other substances, e. g. zinc sulphate is classified in D11AX04 - *Lithium succinate*.

Diclofenac formulated as a 3 % hyaluronic acid gel used in treatment of actinic keratoses is classified here.

G GENITO URINARY SYSTEM AND SEX HORMONES

G01 GYNECOLOGICAL ANTIINFECTIVES AND ANTISEPTICS

A Antiinfectives and antiseptics, excl. combinations with corticosteroids

B Antiinfectives/antiseptics in combination with corticosteroids

G02 OTHER GYNECOLOGICALS

A Oxytocics

B Contraceptives for topical use

C Other gynecologicals

G03 SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM

A Hormonal contraceptives for systemic use

B Androgens

C Estrogens

D Progestogens

E Androgens and female sex hormones in combination

F Progestogens and estrogens in combination

G Gonadotropins and other ovulation stimulants

H Antiandrogens

X Other sex hormones and modulators of the genital system

G04 UROLOGICALS

B Other urologicals, incl. antispasmodics

C Drugs used in benign prostatic hypertrophy

G GENITO URINARY SYSTEM AND SEX HORMONES

G01 GYNECOLOGICAL ANTIINFECTIVES AND ANTISEPTICS

This group comprises gynecological antiinfectives and antiseptics mainly for local use. See also:

- J - *Antiinfectives for systemic use*
- D06 - *Antibiotics and chemotherapeutics for dermatological use*
- P01AB - *Nitroimidazole derivatives*

The DDDs are based on the treatment of vaginal infections.

G01A ANTIINFECTIVES AND ANTISEPTICS, EXCL. COMBINATIONS WITH CORTICOSTEROIDS

This group comprises preparations, mainly for local use.

Combinations with corticosteroids, see G01B.

Antivirals for topical use, including gynecological use, such as podophyllotoxin, are classified in D06 - *Antibiotics and chemotherapeutics for dermatological use*.

G01AA Antibiotics

G01AB Arsenic compounds

G01AC Quinoline derivatives

G01AD Organic acids

G01AE Sulfonamides

Combinations of different sulfonamides are given the code G01AE10.

G01AF Imidazole derivatives

Imidazole derivatives (e.g. metronidazole and ornidazole) in formulations for vaginal administration are classified in this group. Parenteral formulations are classified in J01XD, as they are mainly used in anaerobic infections. Imidazole derivatives in oral (including tablets used for the treatment of gynecological infections only) and rectal dosage forms are classified in P01AB. Metronidazole for topical use in skin disorders is classified in D06BX - *Other chemotherapeutics*.

G01AG Triazole derivatives

Fluconazole tablets in single dose packages, only for gynecological infections, are classified together with other packages for systemic use in J02A - *Antimycotics for systemic use*.

G01AX Other antiinfectives and antiseptics

G01B ANTIINFECTIVES/ANTISEPTICS IN COMBINATION WITH CORTICOSTEROIDS

All antiinfectives/antiseptics for gynecological use, which contain corticosteroids, are classified in this group.

G01BA Antibiotics and corticosteroids

G01BC Quinoline derivatives and corticosteroids

G01BD Antiseptics and corticosteroids

G01BE Sulfonamides and corticosteroids

G01BF Imidazole derivatives and corticosteroids

G02 OTHER GYNECOLOGICALS

Analgesics used in dysmenorrhea, see N02B - *Other analgesics and antipyretics* and M01A - *Antiinflammatory and antirheumatic products, non-steroids*.

G02A OXYTOCICS

Plain preparations of oxytocin and analogues are classified in H01B - *Posterior pituitary lobe hormones*.

G02AB *Ergot alkaloids*

This group comprises ergot alkaloids, e.g. methylergometrine, used for stimulation of uterine contractions. Other ergot alkaloids are classified in C04A - *Peripheral vasodilators*, and in N02C - *Anti-migraine preparations*.

The DDDs are based on use in delivery.

G02AC *Ergot alkaloids and oxytocin incl. analogues, in combination*

G02AD *Prostaglandins*

This group comprises prostaglandins used in e.g. termination of pregnancy.

The DDDs are based on use in termination of pregnancy.

G02AX *Other oxytocics*

This group comprises oxytocics, which cannot be classified in the preceding groups.

G02B CONTRACEPTIVES FOR TOPICAL USE

Contraceptives for systemic use, see G03A.

G02BA *Intrauterine contraceptives*

IUDs (intrauterine devices) are classified in this group. IUDs containing progestogens are also classified in this group.

G02BB *Intravaginal contraceptives*

Pessaries, vaginal foams etc. are classified in this group.

Intravaginal devices containing hormones are also classified in this group.

The DDDs for combined devices containing estrogen and progestogen are based on use in menstrual cycles of 28 days. Thus the DDD is 0.0357 UD (1 UD = 1 device).

G02C OTHER GYNECOLOGICALS

G02CA *Sympathomimetics, labour repressants*

This group includes sympathomimetics used to repress labour. Similar adrenergic drugs, which are mainly used in the treatment of asthma, are classified in R03C.

Fenoterol infusion only intended for repressing preterm labour is classified in this group, while other systemic formulations of fenoterol are classified in R03CC04.

The DDDs are based on use as labour repressants.

G02CB *Prolactine inhibitors*

Cabergoline and bromocriptine low dose tablets are classified in this group. Cabergoline and bromocriptine tablets in higher strengths are classified in N04 - *Anti-Parkinson drugs*.

Lisuride tablets in high strength (0.2 mg) are classified in this group, while low strength tablets (25 mcg) are classified in N02C - *Antimigraine preparations*.

The DDDs are based on use as lactation inhibitors. The DDD for parenteral depot formulations of bromocriptine is equal to the DDD for oral administration, based on the assumption that the single dose parenteral treatment equals 14 days of oral treatment.

G02CC *Antiinflammatory products for vaginal administration*

This group comprises e.g. non-steroidal antiinflammatory drugs for vaginal administration.

G02CX *Other gynecologicals*

G03 **SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM**

Other hormones, see H - *Systemic hormonal preparations, excl. sex hormones and insulins*.

Sex hormones used only in the treatment of cancer (often selected strengths) are classified in L - *Antineoplastic and immunomodulating agents*.

The DDDs of many of the hormone preparations may vary considerably with the route of administration due to substantial differences in bioavailability. The DDDs of depot preparations are calculated as the dose divided by the dosing interval.

G03A **HORMONAL CONTRACEPTIVES FOR SYSTEMIC USE**

This group comprises hormonal preparations, which are used as contraceptives. Similar hormonal preparations, which are used for the treatment of e.g. menopausal symptoms and menstrual irregularities, are classified in G03F.

Combinations of cyproterone and estrogen also used as contraceptives are, however, classified in G03HB.

Intravaginal and intrauterine devices containing hormones are classified in G02B.

Transdermal patches for contraception are classified here.

The DDDs are based on use as contraceptives.

The DDDs of combined preparations of estrogen and progestogen and plain progestogen products are based on use in menstrual cycles of 28 days. Thus, the DDD is 0.75 and 1 UD for 21 and 28 tablets cycle package, respectively.

The same principle is used for transdermal patches.

The DDDs for preparations only used in postcoital contraception are based on the course dose.

G03AA Progestogens and estrogens, fixed combinations

This group comprises preparations, which contain fixed combinations of progestogen and estrogens.

The preparations are classified at 5th levels according to the progestogen.

G03AB Progestogens and estrogens, sequential preparations

This group comprises preparations with varying contents of progestogens and estrogens adjusted to the normal hormonal cycle. A package which is intended for one cycle, may contain e.g. three types of tablets, each designed to cover a special part of the menstrual period. Cycle packages may contain some tablets with progestogen only.

5th levels are built up as in G03AA.

G03AC Progestogens

This group includes hormonal contraceptives, which contain progestogens only.

G03AD Emergency contraceptives

Levonorgestrel products (packages) indicated only for emergency contraception are classified in G03AD01.

G03B ANDROGENS

Anabolic steroids, see A14A. Norethandrolone, which has both anabolic and androgenic effects, is classified in A14A since the anabolic effect is considered to be the most important effect.

This group comprises male sex hormones. Combined preparations are included in this group, except combinations with female sex hormones, which are classified in G03E - *Androgens and female sex hormones in combination*.

The group is subdivided according to chemical structure.

The DDDs are based on use in substitution therapy in male hypogonadism. The DDDs for patches (e.g. testosterone) are given in amount delivered.

G03BA 3-oxoandrosten (4) derivatives

The DDD for parenteral and oral testosterone is expressed as declared amount of ester e.g. undecanoate. The DDD for TD and SL route of administration is expressed as declared amount of testosterone.

G03BB 5-androstanon (3) derivatives

G03C ESTROGENS

This group comprises estrogens and combinations, except combinations with

- androgens, see G03E
- progestogens, see G03F
- antiandrogens, see G03HB

Hormonal contraceptives, see G03A.

Estrogens used only in neoplastic diseases, see L - *Antineoplastic and immunomodulating agents*.

The DDDs are based on systemic use in postmenopausal estrogen substitution therapy and in the treatment of premenstrual ailments. However, for some preparations for vaginal administration the DDDs are based on local treatment.

The DDDs for transdermal preparations are based on the amount of active ingredient delivered per 24 hours and the number of days each patch is used.

G03CA Natural and semisynthetic estrogens, plain

This group comprises preparations, which contain one or more natural or semisynthetic estrogen. Estradiol/polyestradiol are classified at the same 5th level. The same applies to estriol/polyestriol. Combinations of estradiol and estriol are classified in G03CA53.

Combinations with other drugs, see G03CC.

Estropipate is classified in G03CA07 - *estrone*.

The DDD for nasal administration of estradiol is based on daily treatment. No DDD for estradiol vaginal ring has been established.

G03CB Synthetic estrogens, plain

This group comprises preparations, which contain synthetic estrogens only.

Combinations with other drugs, see G03CC.

G03CC Estrogens, combinations with other drugs

This group includes combined preparations with natural, semisynthetic or synthetic estrogens and other drugs.

G03CX Other estrogens

Tibolone is classified in this group even though the chemical structure is different from the other estrogens.

G03D PROGESTOGENS

This group comprises progestogens and combinations, except combinations with

- androgens, see G03E
- estrogens, see G03F

Hormonal contraceptives, see G03A

IUDs (intrauterine devices) with progestogens, see G02BA.

Progestogens only used in neoplastic diseases, see L - *Antineoplastic and immunomodulating agents*.

The group is subdivided according to chemical structure.

The DDDs are based on gynecological indications, for instance corpus luteum insufficiency and endometriosis.

G03DA Pregnen (4) derivatives

G03DB Pregnadien derivatives

G03DC Estren derivatives

Tibolone is classified in G03CX.

G03E ANDROGENS AND FEMALE SEX HORMONES IN COMBINATION

This group comprises preparations with androgen and estrogen and/or progestogen. The preparations are classified at 5th levels according to the androgen.

The DDDs are based on the treatment of climacterical ailments.

G03EA Androgens and estrogens

G03EB Androgen, progestogen and estrogen in combination

G03EK Androgens and female sex hormones in combination with other drugs

This group comprises preparations, which in addition to the hormones also contain other drugs.

G03F PROGESTOGENS AND ESTROGENS IN COMBINATION

This group comprises combined preparations used in the treatment of menopausal symptoms, menstrual irregularities etc.

Hormonal contraceptives, see G03A.

The DDDs for combined preparations of estrogens and progestogens are based on use in postmenopausal substitution therapy in cycles of 28 days. Thus, the DDD is 0.75 and 1 UD for 21 and 28 tablets cycle packages, respectively.

G03FA Progestogens and estrogens, fixed combinations

This group comprises preparations, which contain combinations of progestogens and estrogens. Sequential preparations are classified in G03FB. Combination packages with separate tablets containing progestogens and estrogens intended to be taken together are also classified in this group. The preparations are classified at 5th levels according to the progestogen. At each 5th level various estrogens may occur.

Combinations of progestogens and estrogens used as contraceptives are classified in G03A.

G03FB Progestogens and estrogens, sequential preparations

This group comprises preparations with varying contents of progestogens and estrogens adjusted to the normal hormonal cycle. A

package which is intended for one cycle, may contain e.g. three types of tablets, each designed to cover a special part of the menstrual period. Cycle packages may contain some tablets with progestogens only. Combination packages with separate tablets containing progestogens and estrogens intended to be taken together and in sequence are also classified in this group.

5th levels are built up as in G03FA.

Hormonal contraceptives, sequential preparations, see G03AB.

G03G GONADOTROPINS AND OTHER OVULATION STIMULANTS

The DDDs are based on the initial treatment of anovulation.

G03GA Gonadotropins

This group comprises both naturally occurring gonad-stimulating hormones and synthetic ovulation stimulants. The combination of Follicle Stimulating Hormone and Luteinizing Hormone is classified in G03GA30.

G03GB Ovulation stimulants, synthetic

G03H ANTIANDROGENS

G03HA Antiandrogens, plain

Finasteride used for treatment of benign prostatic hypertrophy is classified in G04CB.

The DDDs are based on the treatment of hypersexualism.

G03HB Antiandrogens and estrogens

This group comprises all combinations of cyproterone and estrogen regardless of indication.

The DDDs are based on the treatment of hirsutism or prophylaxis of postmenopausal osteoporosis.

G03X OTHER SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM

This group comprises drugs modifying the genital functions, which cannot be classified in the preceding groups.
Tibolone is classified in G03DC.

G03XA Antigonadotropins and similar agents

The DDDs of danazol and gestrinone are based on the treatment of endometriosis.

G03XB Antiprogestogens

G03XC Selective estrogen receptor modulators

G04 UROLOGICALS

Antiseptic and antiinfective preparations for systemic use specifically used in urinary tract infections, see J01.

Antiinfectives for systemic use, see group J.

Gynecological antiinfectives and antiseptics, see G01.

G04B OTHER UROLOGICALS, INCL. ANTISPASMODICS

This group comprises urological preparations other than antiseptics and antiinfectives.

G04BA Acidifiers

G04BC Urinary concrement solvents

This group comprises agents, which dissolve urinary concrements, e.g. citrates.

G04BD Urinary antispasmodics

This group comprises antispasmodics specifically used in the urogenital tractus.

Gastrointestinal antispasmodics, see A03.

Trospium in combination with analgesics are classified in A03DA.

The DDD for oral administered emeperonium is higher than the DDD for parenteral administered formulations, due to low oral bioavailability.

G04BE Drugs used in erectile dysfunction

Alprostadil intracavernosal injection for treatment of erectil dysfunction is classified here, while formulations used to maintain the patency of the ductus arteriosis in neonates are classified in C01EA01.

Combinations of papaverine and phentolamine for intracavernous administration are classified under G04BE30 - *combinations*.

Combinations of phentolamine and aviptadil (polypeptide) are classified under G04BE30 - *combinations*.

The DDDs are based on single treatment of erectile dysfunction.

G04BX Other urologicals

This group comprises urologicals which cannot be classified in the preceding groups.

Phenazopyridine, plain products, are classified here, while phenazopyridine in combination with sulfonamides is classified according to the sulfonamide in J01EB20, J01EC20 or J01ED20.

The DDD of phenazopyridine is based on analgesic treatment of conditions such as cystitis, prostatitis and urethritis. The DDD for phenylsalicylate is based on the prophylaxis of urinary tract infections. The other DDDs are based on the prophylaxis of urinary concretions.

G04C DRUGS USED IN BENIGN PROSTATIC HYPERTROPHY

G04CA Alpha-adrenoreceptor antagonists

Alfuzosin and terazosin used in the management of urinary obstruction caused by benign prostatic hypertrophy, are classified here, while other alpha-adrenoreceptor blocking agents used both in the management of urinary obstruction and hypertension (e.g. doxazosin) are classified in C02CA.

G04CB Testosterone-5-alpha reductase inhibitors

Combinations/combo packages with alpha-adrenoreceptor antagonists are classified in G04CA.

G04CX Other drugs used in benign prostatic hypertrophy

H SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS

H01 PITUITARY AND HYPOTHALAMIC HORMONES AND ANALOGUES

- A Anterior pituitary lobe hormones and analogues*
- B Posterior pituitary lobe hormones*
- C Hypothalamic hormones*

H02 CORTICOSTEROIDS FOR SYSTEMIC USE

- A Corticosteroids for systemic use, plain*
- B Corticosteroids for systemic use, combinations*
- C Antiadrenal preparations*

H03 THYROID THERAPY

- A Thyroid preparations*
- B Antithyroid preparations*
- C Iodine therapy*

H04 PANCREATIC HORMONES

- A Glycogenolytic hormones*

H05 CALCIUM HOMEOSTASIS

- A Parathyroid hormones and analogues*
- B Anti-parathyroid agents*

H SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS

This group comprises all hormonal preparations for systemic use, except:

- Insulins, see A10.
- Anabolic steroids, see A14.
- Catecholamines, see C01C and R03C.
- Sex hormones, see G03.
- Sex hormones used in treatment of neoplastic diseases, see L02.

The DDDs are generally based on the treatment or diagnosis of endocrine disorders.

H01 PITUITARY AND HYPOTHALAMIC HORMONES AND ANALOGUES

H01A ANTERIOR PITUITARY LOBE HORMONES AND ANALOGUES

This group comprises anterior pituitary lobe hormones; extracts, purified natural hormones and synthetic analogues.

Somatropin antagonists are classified in H01AX.

H01AA ACTH

This group comprises ACTH and synthetic analogues.

The DDD of corticotrophin is based on therapy, whereas that of tetracosactide is based on use as a diagnostic agent.

H01AB Thyrotropin

H01AC Somatropin and somatropin agonists

Mecasermin (insulin like growth factor) is classified in this group since it is used on the same indications as somatropin and somatrem. High strength preparations of sermorelin are classified here. Low strength preparations used as diagnostic agents for pituitary function are classified in V04CD.

The DDDs are based on the treatment of growth retardation in children with a body weight of 25 kg.

H01AX Other anterior pituitary lobe hormones and analogues

Somatropin antagonists are classified here.

H01B POSTERIOR PITUITARY LOBE HORMONES

This group comprises posterior pituitary lobe hormones; extracts, purified natural hormones and synthetic analogues.

H01BA Vasopressin and analogues

The DDDs are based on the treatment of diabetes insipidus.

H01BB Oxytocin and analogues

Oxytocin and analogues in combination with ergot alkaloids are classified in G02A - *Oxytocics*

The DDDs are based on use in delivery.

H01C HYPOTHALAMIC HORMONES

This group comprises hypothalamic hormones; extracts, purified natural hormones and synthetic analogues.

Hypothalamic hormones used as diagnostic agents for pituitary function are classified in V04CD.

H01CA Gonadotropin-releasing hormones

Gonadotropin-releasing hormones used for neoplastic diseases are classified in L02A - *Hormones and related agents*.

Gonadorelin used as diagnostic agent is classified in V04CM.

The DDD of nafarelin is based on the treatment of endometriosis. No other DDDs have been assigned, due to the highly variable dosages used.

H01CB Antigrowth hormones

Somatostatin, octreotide and lanreotide, which are also used in cancer, are classified in this group.

The DDDs of octreotide and lanreotide are based on the treatment of acromegaly.

H01CC Anti-gonadotropin-releasing hormones

H02 CORTICOSTEROIDS FOR SYSTEMIC USE

As a main rule, systemic corticosteroids should be classified in this group. There is, however, one exception: M01BA - *Antiinflammatory/antirheumatic agents in combination with corticosteroids*.

Corticosteroids for local oral treatment, see A01AC.

Enemas and rectal foams for local treatment of e.g. ulcerative colitis, see A07E.

Corticosteroids for topical use, see D07.

Combined corticosteroid preparations for local treatment of acne, see D10AA.

Corticosteroids in combination with antiinfectives/antiseptics for local treatment of gynecological infections, see G01B.

Corticosteroids for nasal use, see R01AD.

Corticosteroids for inhalation, see R03BA.

Corticosteroids, eye/ear preparations, see S.

H02A CORTICOSTEROIDS FOR SYSTEMIC USE, PLAIN

Only plain preparations are classified in this group. The group also includes corticosteroid preparations for local injection.

H02AA Mineralocorticoids

The DDDs are based on substitution therapy in Addison's disease.

H02AB Glucocorticoids

Oral formulations used solely in local treatment are classified in A07EA.

Depot preparations may have different DDDs, compared to other formulations, due to different indications.

H02B CORTICOSTEROIDS FOR SYSTEMIC USE, COMBINATIONS

This group comprises all combined preparations, e.g. combinations with local anesthetics.

No DDDs have been assigned.

H02BX Corticosteroids for systemic use, combinations

H02C ANTIADRENAL PREPARATIONS

H02CA Anticorticosteroids

Trilostane used in Cushing's syndrome is classified in this group.

The DDD of trilostan is based on the treatment of Cushing's syndrome.

H03 **THYROID THERAPY**

H03A **THYROID PREPARATIONS**

This group comprises thyroid extracts and synthetic analogues used in the treatment of hypothyrosis.

The DDDs are based on the treatment of hypothyrosis.

H03AA Thyroid hormones

This group comprises natural and synthetic thyroid hormones. Combinations of levothyroxine and liothyronine are classified at a separate 5th level: H03AA03.

H03B **ANTITHYROID PREPARATIONS**

This group comprises preparations used in the treatment of hyperthyrosis.

The DDDs are based on the treatment of hyperthyrosis.

H03BA Thiouracils

H03BB Sulfur-containing imidazole derivatives

H03BC Perchlorates

H03BX Other antithyroid preparations

H03C **IODINE THERAPY**

This group comprises iodine preparations for systemic use.

H03CA Iodine therapy

The DDDs are based on systemic therapy in thyroid disease. The DDD is given in amount of iodide.

H04 PANCREATIC HORMONES

H04A GLYCOGENOLYTIC HORMONES

H04AA Glycogenolytic hormones

The pancreas glycogenolytic hormone glucagon is classified in this group.

Diazoxide, which is also used for treatment of hypoglycemia, is classified in C02DA01 and V03AH01.

Insulins are classified in A10A.

The DDD of glucagon is based on single dose treatment of hypoglycemia.

H05 CALCIUM HOMEOSTASIS

Drugs acting on calcium homeostasis are classified in this group.

Vitamin-D preparations, see A11CC.

H05A PARATHYROID HORMONES AND ANALOGUES

H05AA Parathyroid hormones and analogues

Extracts from parathyroid glands are classified in this group.

H05B ANTI-PARATHYROID AGENTS

H05BA Calcitonin preparations

Calcitonin, natural and synthetic, is classified in this group. Other drugs for treatment of hypercalcemia, see M05B.

The DDDs of the calcitonins are based on the treatment of Paget's disease.

H05BX Other anti-parathyroid agents

Paricalcitol and doxercalciferol indicated for the prevention and treatment of secondary hyperparathyroidism are classified here.

J ANTIINFECTIVES FOR SYSTEMIC USE

J01 ANTIBACTERIALS FOR SYSTEMIC USE

- A Tetracyclines*
- B Amphenicols*
- C Beta-lactam antibacterials, penicillins*
- D Other beta-lactam antibacterials*
- E Sulfonamides and trimethoprim*
- F Macrolides, lincosamides and streptogramins*
- G Aminoglycoside antibacterials*
- M Quinolone antibacterials*
- R Combinations of antibacterials*
- X Other antibacterials*

J02 ANTIMYCOTICS FOR SYSTEMIC USE

- A Antimycotics for systemic use*

J04 ANTIMYCOBACTERIALS

- A Drugs for treatment of tuberculosis*
- B Drugs for treatment of lepra*

J05 ANTIVIRALS FOR SYSTEMIC USE

- A Direct acting antivirals*

J06 IMMUNE SERA AND IMMUNOGLOBULINS

- A Immune sera*
- B Immunoglobulins*

J07 VACCINES

- A Bacterial vaccines*
- B Viral vaccines*
- C Bacterial and viral vaccines, combined*
- X Other vaccines*

J ANTIINFECTIVES FOR SYSTEMIC USE

Antiinfectives are also classified in the following groups:

- A01AB *Antiinfectives and antiseptics for local oral treatment*
- A02BD *Combinations for eradication of *Helicobacter pylori**
- A07A *Intestinal antiinfectives*
- D01 *Antifungals for dermatological use*
- D06 *Antibiotics and chemotherapeutics for dermatological use*
- D07C *Corticosteroids, combinations with antibiotics*
- D09AA *Ointment dressings with antiinfectives*
- D10AF *Antiinfectives for treatment of acne*
- G01 *Gynecological antiinfectives and antiseptics*
- P *Antiparasitic products, insecticides and repellents*
- R02AB *Antibiotics*
- R05X *Other cold combination preparations*
- S01/
S02/
S03 *Eye and ear preparations with antiinfectives*

Even systemically administered antibacterials and antimycotics may be classified in other groups if their target is exclusively local, e.g. the skin - D01 - *Antifungals for dermatological use*

Inhaled antiinfectives are classified in J.

The DDDs for the antiinfectives are as a main rule based on the use in infections of moderate severity. However, some antiinfectives are only used in severe infections and their DDDs are assigned accordingly. The DDDs assigned are based on **daily treatment**. The duration of the treatment periods is not taken into consideration. For antiinfectives given in a high initially starting dose followed by a lower daily "maintenance" dose, the DDDs are based on the "maintenance" dose if the total duration of the treatment course is more than one week. If, however, the treatment course is 7 days or less, the DDDs are assigned according to the average daily dose i.e. the total course dose divided by the number of treatment days (e.g. azithromycin).

J01 ANTIBACTERIALS FOR SYSTEMIC USE

This group comprises antibacterials for systemic use, except antimycobacterials, which are classified in J04. The antibacterials are classified according to their mode of action and chemistry.

Combinations of two or more systemic antibacterials from different third levels are classified in J01R, except combinations of sulfonamides and trimethoprim, which are classified at a separate 4th level, J01EE.

Combinations of antibacterials with other drugs, including local anesthetics or vitamins, are classified at separate 5th levels in the respective antibacterial group by using the 50-series. Common cold preparations containing minimal amounts of antibacterials are classified in R05X.

Inhaled antiinfectives are classified here based on the fact that preparations for inhalation can not be separated from preparations for injection.

J01A TETRACYCLINES

J01AA Tetracyclines

This group comprises tetracycline antibacterials inhibiting the bacterial protein synthesis through binding to the 30-S part of ribosomes.

The tetracyclines have different DDDs due to kinetic differences. The use of tetracyclines in long-term, low dose treatment of acne is not taken into account in the assignment of DDDs.

J01B AMPHENICOLS

J01BA Amphenicols

This group comprises amphenicol antibacterials inhibiting the bacterial protein synthesis.

Thiamphenicol acetylcysteinate glycinate for inhalation is classified in J01BA52.

J01C BETA-LACTAM ANTIBACTERIALS, PENICILLINS

This group comprises penicillin beta-lactam antibacterials, inhibiting the bacterial cell wall synthesis. Combinations of penicillins from different 4th levels, including beta-lactamase inhibitors, are classified in J01CR.

J01CA Penicillins with extended spectrum

This group comprises penicillins with enhanced activity against gram negative rods, e.g. ampicillin and similar antibiotics.

The esters, for instance pivampicillin and pivmecillinam, have a higher bioavailability and thus a lower DDD than the corresponding non-ester compounds.

The DDDs for some of the compounds, for instance carbenicillin, piperacillin, ticarcillin and sulbenicillin, are based on the dosages used for narrow indications, i.e. life threatening infections.

J01CE Beta-lactamase sensitive penicillins

Benzylpenicillin and phenoxymethylpenicillin have different DDDs due to differences in indications, route of administration and bioavailability. The DDDs for the combination of benzylpenicillin and procaine penicillin is based on the treatment of syphilis, see list of DDDs for combination products, www.whocc.no.

J01CF Beta-lactamase resistant penicillins

J01CG Beta-lactamase inhibitors

The DDD for sulbactam is based on its use together with ampicillin, usually in a dose ratio of 1:2 respectively.

J01CR Combinations of penicillins, incl. beta-lactamase inhibitors

This group comprises combinations of penicillins and/or beta-lactamase inhibitors. Combinations containing one penicillin and enzyme inhibitor are classified at different 5th levels according to the penicillin. Combinations of two or more penicillins with or without enzyme

inhibitor are classified at a separate 5th level, J01CR50. Sultamicillin, a prodrug for sulbactam and ampicillin, is given a separate 5th level code: J01CR04.

The DDD for sultamicillin, a prodrug for sulbactam and ampicillin, is lower than the corresponding DDD for the ordinary combination due to higher bioavailability.

J01D OTHER BETA-LACTAM ANTIBACTERIALS

This group comprises beta-lactam antibacterials, other than penicillins.

The cephalosporins are classified into subgroups according to generations. The reference applied when defining generations is “Principles and Practice of Infectious Diseases” by Mandell, Douglas and Benett, sixth edition, 2005. For the definitions used in this textbook, see under J01DB, J01DC, J01DD and J01DE.

The cephalosporins are used in highly variable dosages for different indications, which should be reflected in the assigned DDDs. The indications for use of the cephalosporins (i.e. the severity of the infections) vary rather extensively from one country to another. The assigned DDDs are placed in the upper area of the dose range for moderate to severe infections.

J01DB First-generation cephalosporins

The first generation compounds have relatively narrow spectrum of activity focused primarily on the gram-positive cocci.

J01DC Second-generation cephalosporins

The second generation cephalosporins have a variable activity against gram-positive cocci but have increased activity against gram-negative bacteria. The cephamycin group is included in the second-generation cephalosporins.

J01DD Third-generation cephalosporins

The third generation cephalosporins have a marked activity against gram-negative bacteria. Limited activity against gram-positive cocci,

particularly methicillin susceptible *S. aureus*, might occur.

J01DE Fourth-generation cephalosporins

The fourth generation cephalosporins have activity against gram-positive cocci and a broad array of gram-negative bacteria, including *P. aeruginosa* and many of the Enterobacteriaceae with inducible chromosomal β -lactamases.

J01DF Monobactams

Arginin and lysine salts of aztreonam are classified in J01DF01; thus aztreonam for inhalation is classified together with systemic formulations.

J01DH Carbapenems

Combinations with enzyme inhibitors are classified at separate 5th levels, using the 50-series.

J01DI Other cephalosporins

J01E SULFONAMIDES AND TRIMETHOPRIM

This group comprises systemic sulfonamide and trimethoprim preparations. Combinations of sulfonamide and trimethoprim are classified in J01EE. Preparations containing two or more sulfonamides are classified within the different 4th levels, using the 5th level code 20.

In such combinations, the half-life of the most long-acting sulfonamide determines the classification. Sulfonamides in combinations with other antibacterials (excl. trimethoprim) are classified in J01R. Dapsone is classified in J04 - *Antimycobacterials*. See also A07A - *Intestinal antiinfectives*.

Preparations, which in addition contain a urine acidifier, such as vitamin C, calcium- or ammonium chloride, are classified at the plain 5th levels.

The DDDs for the sulfonamides are related to the duration of effect, i.e. usually the long-acting sulfonamides will have lower DDDs than the short-acting.

J01EA Trimethoprim and derivatives

The DDDs are based on the treatment of acute urinary-tract infections.

J01EB Short-acting sulfonamides

This group comprises sulfonamides with a biological half-life not exceeding approx. 7 hours.

J01EC Intermediate-acting sulfonamides

This group comprises sulfonamides with a biological half-life of approx. 11-12 hours.

J01ED Long-acting sulfonamides

This group comprises sulfonamides with a biological half-life of approx. 35 hours or more.

J01EE Combinations of sulfonamides and trimethoprim, incl. derivatives

When establishing DDDs for combination products, both components are taken into consideration, see list of DDDs for combination products, www.whooc.no.

J01F MACROLIDES, LINCOSAMIDES AND STREPTOGRAMINS

This group comprises macrolide, lincosamide and streptogramin antibacterials inhibiting bacterial protein synthesis through binding to the 50-S part of the ribosomes.

J01FA Macrolides

Erythromycin ethylsuccinate tablets have been assigned a higher DDD than other preparations of erythromycin due to a lower bioavailability. This DDD is mainly based on the dose recommendations.

The oral DDD for azithromycin is based on a 5-day regimen.

J01FF Lincosamides

Orally and parenterally administered clindamycin have different DDDs due to different indications, i.e. the intestinal and systemic infections, respectively.

J01FG Streptogramins

The streptogramin components dalfopristin/quinupristin are semisynthetic derivatives of pristinamycin. The two components have synergistic antibacterial effect and are always used together. Quinupristin/dalfopristin are therefore classified at the ATC plain level J01FG02.

J01G AMINOGLYCOSIDE ANTIBACTERIALS

This group comprises aminoglycoside antibacterials disturbing the bacterial protein synthesis through binding to the 30-S part of the ribosomes.

J01GA Streptomycins

Streptomycins in combination with antimycobacterials are classified in J04AM.

J01GB Other aminoglycosides

Tobramycin for inhalation is classified together with systemic formulations in J01GB01.

The DDDs for the aminoglycosides are based on use in severe infections.

J01M QUINOLONE ANTIBACTERIALS

This group comprises quinolone antibacterials, inhibiting the bacterial DNA-gyrase.

J01MA Fluoroquinolones

Flumequine is classified in J01MB.

The DDDs for the fluoroquinolones are mainly based on the treatment of respiratory tract infections. The DDDs for pefloxacin, enoxacin and norfloxacin are based on the treatment of complicated urinary tract infections.

J01MB Other quinolones

Preparations, which in addition contain a urine acidifier, such as vitamin C, calcium- or ammonium chloride, are classified at the plain 5th levels.

The DDDs are generally based on the treatment of acute urinary tract infections. The DDD for rosoxacin is based on single dose treatment of gonorrhoea.

J01R COMBINATIONS OF ANTIBACTERIALS

This group comprises combinations of two or more antibacterials for systemic use from different ATC 3rd levels.

J01RA Combinations of antibacterials

Combinations of urinary antiseptics and antiinfectives are classified in J01RA02.

J01X OTHER ANTIBACTERIALS

This group comprises antibacterials with various modes of action not classified in the preceding groups.

J01XA Glycopeptide antibacterials

This group comprises glycopeptide antibacterials, inhibiting the cell wall synthesis of gram positive bacteria. Teicoplanin and intravenous preparations of vancomycin are classified in this group. Oral formulations containing vancomycin are classified in A07A.

J01XB Polymyxins

This group comprises polymyxin antibacterials acting on the bacterial cytoplasm membrane. Oral formulations containing colistin are classified in A07A.

J01XC Steroid antibacterials

This group comprises steroid antibacterials, inhibiting the binding of bacterial transfer-RNA and the 50-S part of the ribosomes.

J01XD Imidazole derivatives

This group comprises imidazole antibacterials acting through active metabolites in anaerobic bacteria. Only formulations for parenteral use of e.g. metronidazole are classified in this group. Oral formulations and suppositories of imidazole derivatives are classified in P01 - *Antiprotozoals*. Pessaries are classified in G01 - *Gynecological antiinfectives and antiseptics*.

The DDDs for the parenteral imidazole formulations are based on the treatment of anaerobic bacteria infections.

J01XE Nitrofurantoin derivatives

Preparations, which in addition contain a urine acidifier, such as vitamin C, calcium- or ammonium chloride, are classified at the plain 5th levels.

The DDDs are generally based on the treatment of acute urinary tract infections.

J01XX Other antibacterials

Preparations, which in addition contain a urine acidifier, such as vitamin C, calcium- or ammonium chloride, are classified at the plain 5th levels.

The parenteral DDD for fosfomycin is based on the use of a single prophylactic dose in connection with surgery, whilst the oral DDD is based on treatment of uncomplicated lower urinary tract infections.

The DDD for spectinomycin is based on the use of a single dose for treatment of uncomplicated gonorrhoea.

The DDD for methenamine is based on prophylaxis of urinary tract infections. The DDDs for mandelic acid and nitroxoline are based on the treatment of acute urinary tract infections.

J02 ANTIMYCOTICS FOR SYSTEMIC USE

J02A ANTIMYCOTICS FOR SYSTEMIC USE

This group does not include antimycotics specifically for dermatological use even if they are administered systemically (see D01B).

Antimycotics - see also:

A01AB *Antiinfectives and antiseptics for local oral treatment*

A07A *Intestinal antiinfectives*

D01 *Antifungals for dermatological use*

G01 *Gynecological antiinfectives and antiseptics*

Fumagillin used in the treatment of intestinal microsporidiosis is classified in P01AX.

The DDDs are based on the treatment of systemic mycosis.

J02AA Antibiotics

The DDD for amphotericin B is based on the conventional formulation. Dosages of other formulations (e.g. liposomal) of amphotericin B may vary considerably. This should be taken into consideration when comparing drug use.

J02AB Imidazole derivatives

J02AC Triazole derivatives

All oral and parenteral formulations of fluconazole are classified here. Vaginal formulations of triazole derivatives, see G01AG.

J02AX Other antimycotics for systemic use

J04 ANTIMYCOBACTERIALS

This group comprises drugs mainly used for the treatment of tuberculosis or lepra. However, streptomycins are classified in J01G - *Aminoglycoside antibacterials*. Streptomycin in combination with antimycobacterials are classified in J04AM.

J04A DRUGS FOR TREATMENT OF TUBERCULOSIS

The DDDs are based on combination therapy in the treatment of tuberculosis. DDDs for combination products see www.whocc.no.

J04AA Aminosalicylic acid and derivatives

J04AB Antibiotics

This group comprises antibiotics specifically used in tuberculosis, except streptomycin - see comment under J04AM. Other antibiotics, see J01 - *Antibacterials for systemic use*.

J04AC Hydrazides

Combinations of isoniazid and rifampicin or other tuberculostatics are classified in J04AM.

J04AD Thiocarbamide derivatives

J04AK Other drugs for treatment of tuberculosis

J04AM Combinations of drugs for treatment of tuberculosis

Combinations of drugs classified in J04AA - J04AK are classified in this group (e. g. isoniazid + rifampicin). Combinations of antimycobacterials and streptomycin are classified in this group while plain streptomycin is classified in J01GA - *Streptomycins*.

J04B DRUGS FOR TREATMENT OF LEPROSY

J04BA Drugs for treatment of leprosy

Thalidomide, which is also used for treatment of leprosy, is classified in L04AX.

J05 ANTIVIRALS FOR SYSTEMIC USE

This group comprises specific antiviral agents, excl. vaccines.

Antivirals for dermatological use, see D06BB.

Antivirals for ophthalmological use, see S01A - *Antiinfectives*.

Amantadine, which is also used as an antiviral agent, is classified in N04BB.

J05A DIRECT ACTING ANTIVIRALS

This group comprises agents acting directly on the virus.

J05AA Thiosemicarbazones

J05AB Nucleosides and nucleotides excl. reverse transcriptase inhibitors

The combinations of ribavirin and peginterferon alfa-2a or peginterferon alfa-2b are classified in L03AB.

The DDDs for aciclovir, valaciclovir and famciclovir are based on the treatment of herpes zoster infections.

The DDD for ribavirin is based on the treatment of respiratory syncytial viral (RSV) infections in neonates and infants.

The DDD for ganciclovir is based on the treatment of cytomegalovirus infections in immunosuppressed patients.

The DDD for cidofovir is based on the treatment of CMV-retinitis in AIDS patients.

J05AC Cyclic amines

Amantadine is classified in N04 - *Anti-Parkinson drugs*.

J05AD Phosphonic acid derivatives

The DDD for foscarnet is based on the treatment of CMV-retinitis in AIDS patients.

J05AE Protease inhibitors

Ritonavir added as a pharmacokinetic enhancer is allowed in J05AE06 *Lopinavir*.

The DDDs are based on combination therapy in HIV infections.

The DDDs for atazanavir, fosamprenavir and lopinavir are based on combination therapy with ritonavir as a pharmacokinetic enhancer.

The DDD for saquinavir is based on the dose recommendations for hard capsules.

J05AF Nucleoside and nucleotide reverse transcriptase inhibitors

The DDDs are based on combination therapy in HIV infections.

The DDD for tenofovir disoproxil is 245 mg and is equivalent to 300 mg tenofovir disoproxil fumarat.

The DDDs for entecavir and telbivudine are based on monotherapy in the treatment of chronic hepatitis B virus infections.

J05AG Non-nucleoside reverse transcriptase inhibitors

The DDDs are based on combination therapy in HIV infections.

J05AH Neuraminidase inhibitors

All neuraminidase inhibitors are classified here, regardless of formulation.

The DDD of oseltamivir is based on the treatment of influenza.

J05AR Antivirals for treatment of HIV infections, combinations

See list of DDDs for combination products, www.whocc.no.

J05AX Other antivirals

J06 IMMUNE SERA AND IMMUNOGLOBULINS

No DDDs have been assigned, except for nebacumab in J06BC01.

J06A IMMUNE SERA

J06AA Immune sera

This group comprises specific antisera.

J06B IMMUNOGLOBULINS

This group comprises normal human immunoglobulins and specific immunoglobulins.

J06BA Immunoglobulins, normal human

J06BB Specific immunoglobulins

Combinations with vaccines are classified in J07.

J06BC Other immunoglobulins

J07 VACCINES

The vaccines are divided in bacterial, viral and combinations of bacterial and viral at separate ATC 3rd levels. Subdivision at the 4th level is made mainly according to indication, while subdivision at the 5th level

is mainly related to the manufacturing process. Combinations of vaccines within the same 3rd level are given separate 5th levels using the 50-series. 5th levels may contain adjuvans.

See comments under the 4th levels.

No DDDs have been assigned.

J07A BACTERIAL VACCINES

J07AC Anthrax vaccines

J07AD Brucellosis vaccines

J07AE Cholera vaccines

Combinations with typhoid vaccine are classified in this group.

J07AF Diphtheria vaccines

Different strengths of the diphtheria vaccines are classified at the same 5th level. Combinations with tetanus vaccine are classified in J07AM. Combinations with both tetanus and pertussis are classified in J07AJ.

Combinations with hemophilus influenza and tetanus vaccines are classified in J07AG.

Combinations with poliomyelitis and/or rubella are classified in J07CA.

J07AG Hemophilus influenzae B vaccines

Combinations with diphtheria and tetanus vaccines are classified here.

Combinations with pertussis and toxoids are classified here. Combinations with poliomyelitis are classified in J07CA.

J07AH Meningococcal vaccines

Meningococcal vaccines are classified at separate 5th levels according to the number of serotypes of neisseria meningitis contained in the vaccine. Monovalent vaccines obtained from group A are classified at a separate

5th level, while other monovalent vaccines are classified together.

Products containing oligosaccharides instead of polysaccharides may be included at each 5th level.

J07AJ Pertussis vaccines

Combinations with tetanus and/or diphtheria vaccine are classified in this group.

Combinations with hemophilus influenzae B are classified in J07AG.

Combinations with polimyelitis are classified in J07CA.

J07AK Plague vaccines

J07AL Pneumococcal vaccines

J07AM Tetanus vaccines

Combinations with tetanus immunoglobulin are classified in this group. Combinations with diphtheria and/or typhoid vaccines are classified in J07AM51.

Combinations with diphtheria and pertussis vaccines are classified in J07AJ.

Combinations with hemophilus influenza and diphtheria vaccines are classified in J07AG.

Combinations with poliomyelitis and/or rubella are classified in J07CA.

J07AN Tuberculosis vaccines

J07AP Typhoid vaccines

Combinations with tetanus vaccine, also when including diphtheria vaccine, are classified in J07AM.

J07AR Typhus (exanthematicus) vaccines

J07AX Other bacterial vaccines

This group comprises bacterial vaccines, which cannot be classified in the preceding groups, e.g. Q fever vaccine.

J07B VIRAL VACCINES

J07BA Encephalitis vaccines

J07BB Influenza vaccines

Split virus vaccine is classified in J07BB02 together with surface antigen.

J07BC Hepatitis vaccines

Recombinant and plasma derived hepatitis vaccines are classified at the same 5th level.

J07BD Measles vaccines

Combinations with mumps and/or rubella are classified in this group.

J07BE Mumps vaccines

Combinations with measles vaccine, with or without rubella, are classified in J07BD. Combinations with rubella vaccine are classified in J07BJ.

J07BF Poliomyelitis vaccines

Poliomyelitis vaccines are classified according to the number of virus types included and according to administration form, i.e. oral or parenteral.

Combinations with diphtheria/tetanus/pertussis and/or Hemophilus influenzae B are classified in J07CA.

J07BG Rabies vaccines

J07BH Rota virus diarrhea vaccines

J07BJ Rubella vaccines

Combinations with mumps vaccine are classified in this group.
Combinations with measles vaccine, with or without mumps vaccine,
are classified in J07BD.

Combinations with diptheria and tetanus are classified in J07CA.

J07BK Varicella zoster vaccines

J07BL Yellow fever vaccines

J07BM Papillomavirus vaccines

J07BX Other viral vaccines

J07C BACTERIAL AND VIRAL VACCINES, COMBINED

J07CA Bacterial and viral vaccines, combined

Combinations including bacterial and viral vaccines are classified at
separate 5th levels. No specific system for subdivision is established.

J07X OTHER VACCINES

No 4th levels are assigned in this group.

**L ANTINEOPLASTIC AND IMMUNOMODULATING
 AGENTS**

L01 ANTINEOPLASTIC AGENTS

A Alkylating agents

B Antimetabolites

C Plant alkaloids and other natural products

D Cytotoxic antibiotics and related substances

X Other antineoplastic agents

L02 ENDOCRINE THERAPY

A Hormones and related agents

B Hormone antagonists and related agents

L03 IMMUNOSTIMULANTS

A Immunostimulants

L04 IMMUNOSUPPRESSANTS

A Immunosuppressants

L ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS

This group comprises preparations used in the treatment of malignant neoplastic diseases, and immunomodulating agents.

Corticosteroids for systemic use, see H02.

L01 ANTINEOPLASTIC AGENTS

Combination products are classified in L01XY - *Combinations of antineoplastic agents*.

Detoxifying agents used in connection with high dose treatment of antineoplastic agents are classified in V03AF (e.g. calcium folinate)

No DDDs have been established because of highly individualised use and wide dosage ranges. The doses used vary substantially because of various types and severity of neoplastic diseases, and also because of the extensive use of combination therapy.

The consumption of the antineoplastic agents is in some countries measured in grams. This is recommended as a method to be used internationally for these particular agents.

L01A ALKYLATING AGENTS

L01AA Nitrogen mustard analogues

L01AB Alkyl sulfonates

L01AC Ethylene imines

L01AD Nitrosoureas

L01AG Epoxides

L01AX Other alkylating agents

L01B ANTIMETABOLITES

L01BA Folic acid analogues

Trimetrexate is classified in P01AX - *Other agents against amoebiasis and other protozoal agents.*

Methotrexate in oral formulations is classified in L04AX.

L01BB Purine analogues

L01BC Pyrimidine analogues

Fluorouracil for systemic and local treatment is classified here.

L01C PLANT ALKALOIDS AND OTHER NATURAL PRODUCTS

L01CA Vinca alkaloids and analogues

Synthetic analogues are also classified in this group.

L01CB Podophyllotoxin derivatives

Antivirals for topical use, e.g. podophyllotoxin, see D06BB - *Antivirals.*

L01CC Colchicine derivatives

Colchicine is classified in M04AC01.

L01CD Taxanes

L01CX Other plant alkaloids and natural products

L01D CYTOTOXIC ANTIBIOTICS AND RELATED SUBSTANCES

L01DA Actinomycines

L01DB Anthracyclines and related substances

L01DC Other cytotoxic antibiotics

L01X OTHER ANTINEOPLASTIC AGENTS

This group comprises antineoplastic preparations which cannot be classified in the preceding groups.

L01XA Platinum compounds

L01XB Methylhydrazines

L01XC Monoclonal antibodies

Monoclonal antibodies indicated only for the treatment of cancer are classified in L01XC.

Anecortave, indicated for the treatment of exudative age-related macular degeneration, is classified in S01XA – *Other ophthalmologicals*.

L01XD Sensitizers used in photodynamic/radiation therapy

L01XE Protein kinase inhibitors

L01XX Other antineoplastic agents

Also antineoplastic agents for dermatological use are classified here.

L01XY Combinations of antineoplastic agents

All combinations of antineoplastic agents in L01 - *Antineoplastic agents* are classified in this group.

L02 ENDOCRINE THERAPY

Only preparations used specifically in the treatment of neoplastic diseases are classified in this group. This means that some strengths may be classified in this group, while remaining strengths are classified in G03 - *Sex hormones and modulators of the genital system* or H01CA - *Gonadotropin-releasing hormones*.

The DDDs are based on the treatment of cancer (breast-, endometrial, and prostatic).

L02A HORMONES AND RELATED AGENTS

Antigrowth hormones like somatostatin and octreotide, which are also used in the treatment of neoplastic diseases, are classified in H01CB.

L02AA Estrogens

Polyestradiol and combined products, which contain polyestradiol and local anesthetics, are classified at the plain level L02AA02 - *polyestradiol phosphate*.

L02AB Progestogens

L02AE Gonadotropin releasing hormone analogues

L02AX Other hormones

L02B HORMONE ANTAGONISTS AND RELATED AGENTS

L02BA Anti-estrogens

L02BB Anti-androgens

L02BG Enzyme inhibitors

L02BX Other hormone antagonists and related agents

L03 IMMUNOSTIMULANTS

Immunosuppressants, see L04A.

L03A IMMUNOSTIMULANTS

Levamisole, which also affects the immune response, is classified in P02CE.

L03AA Colony stimulating factors

The DDD for pegfilgrastim is based on the declared amount of filgrastim and on the use of one single dose per cycle of chemotherapy. The DDDs for the other G-CSFs are based on daily dosing for six subsequent days.

L03AB Interferons

Peginterferon alfa-2b in combination with ribavirin and peginterferon alfa-2a in combination with ribavirin are classified in L03AB60 and L03AB61, respectively.

The DDD for interferon alfa is based on the treatment of chronic active hepatitis B, whilst the DDD for interferon beta is based on the treatment of multiple sclerosis.

The DDDs of interferon beta-1a is based on i.m. administration.

L03AC Interleukins

L03AX Other immunostimulants

The DDD for tasonermin is based on single dose treatment.

L04 IMMUNOSUPPRESSANTS

Immunosuppressants are defined as agents that completely or partly suppress one or more factors in the immunosystem.

L04A IMMUNOSUPPRESSANTS

This group comprises immunosuppressants excl. corticosteroids.

The DDDs are mainly based on prophylaxis of allograft transplant rejection.

The DDD for muromonab-CD3 is based on combination therapy in acute allograft rejection.

The DDD for efalizumab is based on the treatment of plaque psoriasis.

The DDDs for etanercept, infliximab, leflunomide, anakinra and adalimumab are based on the treatment of rheumatoid arthritis.

The DDD for certolizumab pegol is based on the treatment of Crohn's Disease.

The DDD for thalidomide is based on the treatment of erythema nodosum leprosum.

The DDD for lenalidomide is based on the treatment of myelodysplastic syndromes.

L04AA Selective immunosuppressants

Antilymphocyte immunoglobulin from horse serum is classified in L04AA03.

Antithymocyte immunoglobulin from rabbit serum is classified in L04AA04.

L04AB Tumor necrosis factor alpha (TNF- α) inhibitors

L04AC Interleukin inhibitors

L04AD Calcineurin inhibitors

L04AX Other immunosuppressants

Methotrexate in oral formulations is classified here, other routes of administration, see L01BA.

M MUSCULO-SKELETAL SYSTEM

M01 ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS

- A Antiinflammatory and antirheumatic products, non-steroids*
- B Antiinflammatory/antirheumatic agents in combination*
- C Specific antirheumatic agents*

M02 TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN

- A Topical products for joint and muscular pain*

M03 MUSCLE RELAXANTS

- A Muscle relaxants, peripherally acting agents*
- B Muscle relaxants, centrally acting agents*
- C Muscle relaxants, directly acting agents*

M04 ANTIGOUT PREPARATIONS

- A Antigout preparations*

M05 DRUGS FOR TREATMENT OF BONE DISEASES

- B Drugs affecting bone structure and mineralization*

M09 OTHER DRUGS FOR DISORDERS OF THE MUSCULO-SKELETAL SYSTEM

- A Other drugs for disorders of the musculo-skeletal system*

M MUSCULO-SKELETAL SYSTEM

M01 ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS

M01A ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-STEROIDS

This group comprises antiinflammatory and antirheumatic preparations for systemic use.

The substances in this group have a broad range of indications, however, they should be kept together in M01A.

Corticosteroids, see H02 - *Corticosteroids for systemic use.*

Disease Modifying Antirheumatic Drugs (DMARDs) see:

A07EC - *Aminosalicylic acid and similar agents*

L01BA - *Folic acid analogues*

L04AA - *Selective immunosuppressants*

L04AX - *Other immunosuppressants*

M01C - *Specific antirheumatic agents*

P01BA - *Aminoquinolines*

All preparations containing salicylic acid and derivatives are classified in N02BA - *Salicylic acid and derivatives*, as it is difficult to differentiate between use of salicylates in rheumatic conditions and other therapeutic uses.

Exception: Salicylates in combination with corticosteroids are classified in M01B.

Combinations of antiinflammatory/antirheumatic agents (e.g. corticosteroids) are classified in M01B.

Antiinflammatory or antirheumatic products in combination with other drugs (incl. codeine less than 20 mg per unit) are classified at separate 5th levels using the corresponding 50-series. Combinations with codeine (20 mg or more per unit dose) are classified in N02AA.

Combined cold preparations with therapeutic levels of antiinflammatory agents are classified in this group at separate 5th levels by using the 50-series.

Combinations with drugs classified in A02B (e.g. esomeprazole) are classified in M01A using the 50-series.

The DDDs are based on the treatment of rheumatoid arthritis, except for the coxibs (M01AH).

M01AA Butylpyrazolidines

M01AB Acetic acid derivatives and related substances

M01AC Oxicams

Piroxicam and piroxicam-beta-cyclodextrin are given the same ATC 5th level code M01AC01.

The DDD for meloxicam is based on the treatment of osteoarthritis.

M01AE Propionic acid derivatives

All ibuprofen preparations are classified in this group, even if they are only intended for use as pain relief.

Ketoprofen lysine is classified at the same ATC 5th level as ketoprofen.

M01AG Fenamates

Tolfenamic acid, used in the treatment of migraine, is classified here.

M01AH Coxibs

Celecoxib used in FAP (familial adenomatous polyposis) is classified in L01XX.

The DDDs for the coxibs are based on the treatment of osteoarthritis.

M01AX Other antiinflammatory and antirheumatic agents, non-steroids

This group comprises antiinflammatory and antirheumatic drugs which cannot be classified in the preceding groups.

The DDD for glucosamine refers to glucosamine sulfate.

M01B ANTIINFLAMMATORY/ANTIRHEUMATIC AGENTS IN COMBINATION

M01BA Antiinflammatory/antirheumatic agents in combination with corticosteroids

This group comprises antiinflammatory and antirheumatic drugs in combination with corticosteroids.

Combinations with salicylic acid derivatives are classified in this group.

The preparations are classified at 5th levels according to the anti-inflammatory/analgesic component. At each 5th level, different corticosteroids may occur.

M01BX Other antiinflammatory/antirheumatic agents in combination with other drugs

All combinations of different antiinflammatory agents (excl. corticosteroids) are classified in this group.

M01C SPECIFIC ANTIRHEUMATIC AGENTS

This group comprises specific antirheumatic preparations.

Penicillamine, which is also used in conditions associated with impaired copper metabolism and as an antidot in copper poisoning, is classified in this group regardless of indication.

Other Disease Modifying Antirheumatic Drugs (DMARDs) see:

A07EC - *Aminosalicylic acid and similar agents*

L01BA - *Folic acid analogues*

L04AA - *Selective immunosuppressants*

L04AX - *Other immunosuppressants*

P01BA - *Aminoquinolines*

The DDDs are based on the treatment of rheumatoid arthritis.

M01CA Quinolines

Chloroquine and hydroxychloroquine are classified as antimalaria agents in P01BA.

M01CB Gold preparations

M01CC Penicillamine and similar agents

M01CX Other specific antirheumatic agents

M02 TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN

M02A TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN

This group comprises ointments, liniments, plasters, etc. which may produce symptomatic relief in joint and muscular pain.

No DDDs have been assigned in this group.

M02AA Antiinflammatory preparations, non-steroids for topical use

All non-steroidal antiinflammatory derivatives for topical use are classified here, regardless of indication. Exception is a product containing diclofenac formulated as a 3 % hyaluronic acid gel which is used in treatment of actinic keratoses. This particular formulation is classified in D11AX.

Combinations of non-steroidal antiinflammatory derivatives and other substances for topical use are classified together with plain preparations at the different 5th levels.

M02AB Capsaicin and similar agents

Capsaicin products indicated for the symptomatic treatment of peripheral neuropathic pain (incl. postherpetic neuralgia) are classified in N01BX.

Combined preparations containing nonivamide used as a rubefacient are classified in this group on a 4th level.

M02AC Preparations with salicylic acid derivatives

No separate 5th levels are established in this group.
Combinations of salicylic acid derivatives and other products are classified in this group.

M02AX Other topical products for joint and muscular pain

This group comprises topical products, which cannot be classified in the preceding groups.

Preparations with menthol are generally classified in D04 - *Antipruritics, incl. antihistamines, anesthetics, etc.*

M03 MUSCLE RELAXANTS

This group comprises peripherally, centrally and directly acting muscle relaxants.

See also G04BD - *Urinary antispasmodics.*

M03A MUSCLE RELAXANTS, PERIPHERALLY ACTING AGENTS

This group comprises peripherally acting muscle relaxants such as curare alkaloids and suxamethonium.

The drugs in this group are mainly used together with anesthetics.

As for other drugs used in general anesthesia (see N01A), no DDDs have been established in this group because the doses used vary substantially.

M03AA Curare alkaloids

M03AB Choline derivatives

M03AC Other quaternary ammonium compounds

Sugammadex indicated for reversal of neuromuscular blockade induced by rocuronium or vecuronium is classified in V03AB - *Antidotes*.

M03AX Other muscle relaxants, peripherally acting agents

Botulinum toxin, which is used e.g. for treatment of blepharospasm and hemifacial spasm, is classified in this group.

M03B MUSCLE RELAXANTS, CENTRALLY ACTING AGENTS

This group comprises centrally acting muscle relaxants. Combined preparations are classified at separate 5th levels using the corresponding 50-series (comb. excl. psycholeptics), or the 70-series (comb. with psycholeptics):

The group is subdivided according to chemical structure.

These drugs are used in different conditions associated with pain and rigidity in the muscles, joints etc.

DDDs for combination products, see list on the website www.whooc.no.

M03BA Carbamic acid esters

M03BB Oxazol, thiazine, and triazine derivatives

M03BC Ethers, chemically close to antihistamines

Orphenadrine citrate is classified here. Preparations containing orphenadrine chloride are classified in N04AB.

Combinations with e.g. paracetamol are classified in this group at separate 5th levels by using the 50-series.

M03BX Other centrally acting agents

M03C MUSCLE RELAXANTS, DIRECTLY ACTING AGENTS

This group comprises agents acting directly on the muscles such as dantrolene.

M03CA Dantrolene and derivatives

The DDD of dantrolene is based on the treatment of spasticity after spinal injury.

M04 ANTIGOUT PREPARATIONS

M04A ANTIGOUT PREPARATIONS

The group is subdivided according to mode of action.

The DDDs are based on prophylaxis.

M04AA Preparations inhibiting uric acid production

Combinations of allupurinol and other antigout preparations are classified here.

Rasburicase for the treatment of hyperuricemia is classified in V03AF.

M04AB Preparations increasing uric acid excretion

M04AC Preparations with no effect on uric acid metabolism

M04AX Other antigout preparations

This group comprises preparations which cannot be classified in the preceding groups.

M05 DRUGS FOR TREATMENT OF BONE DISEASES

Drugs used for the treatment of bone diseases, see also:

- A11CC - *Vitamin D and analogues*
- A12A - *Calcium*
- A12CD - *Fluoride*
- G03C/G03F - *Estrogens/Progestogens and estrogens in combination*
- H05BA - *Calcitonins*

M05B DRUGS AFFECTING BONE STRUCTURE AND MINERALIZATION

M05BA *Bisphosphonates*

This group includes plain preparations. Combination packages with calcium for sequential use are classified in M05BB.

The DDDs for the bisphosphonates are based on the treatment of osteoporosis if this is an approved indication.

The DDDs for clodronic acid, pamidronic acid, zoledronic acid, parenteral etidronic acid and parenteral ibandronic acid are based on tumor induced hypercalcemia. The oral DDD for ibandronic acid is based on osteoporosis. Since the duration of the intravenous treatment courses with the bisphosphonates are varying, from 1-5 days, the DDDs for these parenteral formulations are assigned according to the total *course* dose. The DDDs for the oral formulations, which are mainly used for maintenance therapy, are assigned according to *daily* dosages.

The DDDs for alendronic acid, risedronic acid, and oral etidronic acid are based on treatment of osteoporosis.

The DDD for tiludronic acid is based on the treatment of Paget's disease.

M05BB *Bisphosphonates, combinations*

M05BC *Bone morphogenetic proteins*

M05BX Other drugs affecting bone structure and mineralization

The DDD for denosumab is based on the treatment of osteoporosis.

M09 OTHER DRUGS FOR DISORDERS OF THE MUSCULO-SKELETAL SYSTEM

M09A OTHER DRUGS FOR DISORDERS OF THE MUSCULO-SKELETAL SYSTEM

This group comprises preparations used in disorders of the musculo-skeletal system, which cannot be classified in the preceding groups.

M09AA Quinine and derivatives

Hydroquinine, which is used in the treatment of nocturnal leg cramps is classified in this group.

Quinine is classified as an antimalaria agent in P01BC. Quinine in combination with psycholeptics is classified in M09AA72, since these combinations are used for treatment of nocturnal leg cramps.

Combinations used for cold conditions, containing quinine as an antipyretic, are classified in R05X.

M09AB Enzymes

All enzyme preparations, which are used to treat inflammatory conditions in the musculo-skeletal system, are classified in this group.

M09AX Other drugs for disorders of the musculo-skeletal system

Hyaluronic acid injection for intraarticular administration (e.g. 2.5 mg/ampoule) used in the treatment of arthritis is classified in this group. Hyaluronic acid injection used during surgical procedures on the eye (e.g. 4-20 mg/ampoule) is classified in S01K.

The DDD for hyaluronic acid is based on intraarticular treatment of arthritis. The DDD is assigned according to daily dose even if the product is given as weekly injections.

N NERVOUS SYSTEM

N01 ANESTHETICS

A Anesthetics, general

B Anesthetics, local

N02 ANALGESICS

A Opioids

B Other analgesics and antipyretics

C Antimigraine preparations

N03 ANTIEPILEPTICS

A Antiepileptics

N04 ANTI-PARKINSON DRUGS

A Anticholinergic agents

B Dopaminergic agents

N05 PSYCHOLEPTICS

A Antipsychotics

B Anxiolytics

C Hypnotics and sedatives

N06 PSYCHOANALEPTICS

A Antidepressants

B Psychostimulants, agents used for ADHD and nootropics

C Psycholeptics and psychoanaleptics in combination

D Anti-dementia drugs

N07 OTHER NERVOUS SYSTEM DRUGS

A Parasympathomimetics

B Drugs used in addictive disorders

C Antivertigo preparations

X Other nervous system drugs

N NERVOUS SYSTEM

N01 ANESTHETICS

No DDDs have been established in this group because the doses used vary substantially.

N01A ANESTHETICS, GENERAL

This group comprises agents which produce general anesthesia, surgical analgesia or neuroleptanalgesia. See also M03A - *Peripherally acting muscle relaxants*.

Benzodiazepine derivatives are classified in N05BA or N05CD.

N01AA Ethers

N01AB Halogenated hydrocarbons

N01AF Barbiturates, plain

This group comprises barbiturates used as anesthetics.

Barbiturates used as hypnotics/sedatives and as premedication, see N05CA - *Barbiturates, plain*.

N01AG Barbiturates in combination with other drugs

Only preparations used as anesthetics are classified in this group. See also N05CB - *Barbiturates, combinations*.

N01AH Opioid anesthetics

Opioid anesthetics in combination with other anesthetics are classified in this group at separate 5th levels using the corresponding 50-series.

Transdermal formulations of fentanyl are classified in N02AB.

N01AX Other general anesthetics

This group comprises various plain and combined drugs used to produce anesthesia/analgesia, which cannot be classified in the preceding groups.

Oral formulations of droperidol are classified in N05AD.

N01B ANESTHETICS, LOCAL

Local anesthetics in this context mean anesthetics which only affect a local area as opposed to general anesthetics affecting the entire body.

Creams and plasters containing e.g. lidocaine or prilocaine used as anesthetics or analgesics in the skin are classified in N01BB.

Local anesthetics for dermatological use such as treatment of pruritus, minor burns and insect stings are classified in D04AB - *Anesthetics for topical use*.

Antihemorrhoidals containing anesthetics, see C05AD - *Local anesthetics*.

Stomatologicals with anesthetics, see A01AD.

Combinations of corticosteroids and anesthetics, see A01AC.

Throat preparations with anesthetics, see R02AD - *Anesthetics, local*.

Ophthalmological anesthetics, see S01HA.

Combinations with e.g. epinephrine are classified at separate 5th levels by using the 50-series.

N01BA Esters of aminobenzoic acid

Plasters containing lidocaine and tetracaine are classified in N01BB.

N01BB Amides

Lidocaine injections used as antiarrhythmics are classified in C01BB.

N01BC Esters of benzoic acid

N01BX Other local anesthetics

Capsaicin products indicated for the symptomatic treatment of peripheral neuropathic pain (incl. postherpetic neuralgia) are classified in N01BX. See also M02AB.

N02 ANALGESICS

This group comprises general analgesics and antipyretics.

All salicylic acid derivatives except combinations with corticosteroids are classified in N02BA - *Salicylic acid and derivatives*, as it is difficult to differentiate between the use of salicylates in rheumatic conditions and other therapeutic uses of salicylates.

All ibuprofen preparations are classified in M01A, even if they are only intended for use as pain relief.

Salicylic acid derivatives in combination with corticosteroids are classified in M01B.

There are a number of combined preparations, which contain analgesics and psycholeptics. These are classified in N02, as pain relief must be regarded as the main indication. Analgesics used for specific indications are classified in the respective ATC groups. E.g.:

A03D/

A03EA - *Antispasmodic/psycholeptics/analgesic combinations*

M01 - *Antiinflammatory and antirheumatic products*

M02A - *Topical products for joint and muscular pain*

M03 - *Muscle relaxants*

See comments to these groups.

Lidocaine indicated for postherpetic pain is classified in N01BB.

N02A OPIOIDS

This group comprises strong analgesics of the opiate type and analgesics with similar structure or action.

Sufentanil, which is also used as an epidural analgesic, is classified in N01AH.

Combinations with antispasmodics are classified in N02AG.

The DDDs in this group are based on the treatment of pain.

The DDD for oral morphine is higher than the parenteral DDD because of lower bioavailability.

The DDD for combinations of oxycodone and naloxone (N02AA55) is similar to the DDD for plain oxycodone.

N02AA *Natural opium alkaloids*

This group includes natural and semi-synthetic opiates.

Opium, see also A07DA - *Antipropulsives*.

Plain codeine preparations are classified in R05D - *Cough suppressants, excl. combinations with expectorants*. Codeine or dihydrocodeine in combination with other analgesics are classified in this group at separate 5th levels by using the 50-series, if the codeine or dihydrocodeine content is 20 mg or more per unit dose. Combinations with a lower content of codeine or dihydrocodeine are classified at the respective 4th levels in N02B or M01A of the other analgesic components (e.g. paracetamol or acetylsalicylic acid).

Combinations with antihistamines and anticholinergic agents are classified here.

Combinations of oxycodone and naloxone are classified in N02AA55.

The DDDs are based on approved dose recommendations.

When establishing DDDs for combination products in the 50-series, all analgesic components are taken into consideration if the amount of each component is on a therapeutic level.

The DDD, expressed in UD, should normally not exceed the approved dose recommendations for any of the components. See list of DDDs for combination products, www.whooc.no.

N02AB Phenylpiperidine derivatives

Fentanyl patches are classified in this group whereas parenteral formulations are classified in N01AH.

The transdermal DDD for fentanyl is based on the amount delivered per 24 hours.

N02AC Diphenylpropylamine derivatives

Methadone and levacetylmethadol are classified in N07BC - *Drugs used in opioid dependence*.

Dextropropoxyphene in combination with a muscle relaxant is classified in M03B.

Different DDDs are assigned for different dextropropoxyphene salts based on their different solubility.

N02AD Benzomorphan derivatives

N02AE Oripavine derivatives

High strength formulations (above 0.4 mg) of buprenorphine used in opioid dependence are classified in N07BC.

N02AF Morphinan derivatives

N02AG Opioids in combination with antispasmodics

Preparations are classified at 5th levels according to the analgesic. At each level different antispasmodics may occur.

The DDDs in this group are as far as possible equipotent to the DDD for parenteral morphine.

N02AX Other opioids

The group comprises opioids, which cannot be classified in the preceding groups.

N02B OTHER ANALGESICS AND ANTIPYRETICS

See general considerations under N02.

Combinations with opioid analgesics should be classified in N02A at separate 5th levels, using the corresponding 50-series (combinations excl. psycholeptics) or the 70-series (combinations with psycholeptics) or in N02AG - *Opioids in combination with antispasmodics*.

Combinations with codeine or dihydrocodeine are, however, classified in this group if the codeine or dihydrocodeine content per unit dose is less than 20 mg. Otherwise these combinations are classified in N02AA.

Combined preparations which contain more than one analgesic, should be classified by using the following ranking:

1. Phenacetin
2. Bucetin
3. Dipyroceryl
4. Paracetamol
5. Acetylsalicylic acid
6. Phenazone
7. Salicylamide
8. Propyphenazone

This means that a product containing paracetamol and phenazone should be classified in N02BE51 - *paracetamol, combinations excl. psycholeptics* and not in N02BB51 - *phenazone, combinations excl. psycholeptics*.

Dextropropoxyphene plain, and in combination with other analgesics, is classified in N02AC.

Cold preparations with therapeutic levels of analgesics are classified in this group at separate 5th levels by using the 50-series.

Preparations are subdivided on 4th levels according to chemical structure.

Combinations with ascorbic acid (i.e. 50 mg or more per unit dose) are classified at separate 5th levels using the corresponding 50-series. Products containing less than 50 mg per unit dose are classified at the plain level of the analgesic component.

The DDDs are based on approved dose recommendations.

When establishing DDDs for combination products in the 50-series, all analgesic components are taken into consideration if the amount of each component is a therapeutic dose.

The DDD expressed in UD, should normally not exceed the approved dose recommendations for any of the components. See list of DDDs for combinations products, www.whooc.no.

For combination products with codeine (i.e. less than 20 mg per unit dose), the amount of codeine is not taken into account when assigning a DDD.

N02BA Salicylic acid and derivatives

All salicylic acid derivatives including some commonly regarded as non-steroid antiinflammatory drugs, e.g. diflunisal, are classified in this group. See comment under N02 - *Analgesics*.

Salicylic acid derivatives in combination with corticosteroids are classified in M01B. Acetylsalicylic acid preparations specifically intended for use as antithrombotic agents are classified in B01AC.

Lysine acetylsalicylate is classified at the same 5th level as acetylsalicylic acid.

Combinations with antiemetics are classified here.

The DDDs are based on the treatment of pain and not on use in rheumatic diseases.

DDD for combined preparations, see N02B.

N02BB Pyrazolones

N02BE Anilides

Propacetamol, a prodrug of paracetamol is classified at a separate ATC 5th level in this group.

Benorilate, which is an ester of acetylsalicylic acid and paracetamol, is classified in N02BA.

Paracetamol in combination with orphenadrine (citrate) is classified in M03BC.

N02BG Other analgesics and antipyretics

This group comprises analgesics, which cannot be classified in the preceding groups.

The DDD for ziconotide is based on intrathecal administration.

N02C ANTIMIGRAINE PREPARATIONS

This group comprises preparations specifically used in the prophylaxis and treatment of migraine. Analgesics, see N02A and N02B.

Beta blocking agents, see C07.

Antivertigo preparations, see N07.

Cyproheptadine, see R06A - *Antihistamines for systemic use*.

Tolfenamic acid, see M01AG - *Fenamates*.

Indometacin in combination with prochlorperazine and caffeine is classified in M01AB51 – *Indometacin, combinations*.

N02CA Ergot alkaloids

Ergot alkaloids for gynecological use, see G02A and G02CB.

See also C04AE - *Ergot alkaloids*.

Dihydroergotamine, which is also used in the treatment of hypotension, is classified in this group.

Combinations of dihydroergotamine and etilefrine are classified in C01CA.

The DDD for ergotamine is based on the treatment of acute migraine attacks, whereas the DDDs for dihydroergotamine and methysergide are based on prophylaxis.

The DDD for dihydroergotamine nasal spray is based on the treatment of acute migraine attacks.

N02CB Corticosteroid derivatives

The DDDs for corticosteroid derivatives are based on prophylaxis of migraine.

N02CC Selective serotonin (5HT₁) agonists

The DDDs for the selective serotonin (5HT₁) agonists are based on the recommended initial dose in acute attacks of migraine.

N02CX Other antimigraine preparations

This group comprises antimigraine preparations, which cannot be classified in the preceding groups.

Clonidine low strength tablets (e.g. 25 mcg) are classified here, even if the indication also may be “opioid withdrawal symptoms”.

The DDDs for the substances in this group are based on the prophylaxis of migraine.

N03 ANTIEPILEPTICS

N03A ANTIEPILEPTICS

This group comprises preparations used in the treatment of epilepsy.

Combined preparations are classified at separate 5th levels using the corresponding 50-series.

The group is subdivided according to chemical structure.

The DDDs for the antiepileptics are based on combination therapy.

N03AA Barbiturates and derivatives

Barbiturates used mainly as hypnotics/sedatives are classified in N05C - *Hypnotics and sedatives*.

Phenobarbital, which is used both as an antiepileptic and as a sedative, is classified in this group.

Combinations with phenytoin are classified in N03AB.

N03AB Hydantoin derivatives

Combinations of phenytoin and barbiturates are classified in this group.

N03AC Oxazolidine derivatives

N03AD Succinimide derivatives

N03AE Benzodiazepine derivatives

Benzodiazepines with epilepsy as the main indication are classified in this group.

Benzodiazepines mainly used as anxiolytics or hypnotics/sedatives, see N05B and N05C.

N03AF Carboxamide derivatives

N03AG Fatty acid derivatives

N03AX Other antiepileptics

This group comprises antiepileptics, which cannot be classified in the preceding groups.

N04 ANTI-PARKINSON DRUGS

This group comprises preparations used in the treatment of Parkinson's disease and related conditions, including drug-induced parkinsonism.

The DDDs are based on recommended doses for the long-term treatment of symptoms of Parkinson's disease.

No separate DDDs are established for oral depot formulations.

N04A ANTICHOLINERGIC AGENTS

N04AA Tertiary amines

N04AB Ethers chemically close to antihistamines

Orphenadrine chloride is classified in this group, while orphenadrine citrate is classified in M03BC.

N04AC Ethers of tropine or tropine derivatives

N04B DOPAMINERGIC AGENTS

N04BA Dopa and dopa derivatives

Combinations with decarboxylase inhibitors and other dopaminergic agents are classified here.

The DDD for the combination of levodopa and decarboxylase inhibitor is based on the content of levodopa, see ATC index.

N04BB Adamantane derivatives

N04BC Dopamine agonists

Bromocriptine used in parkinsonism is classified in this group (e.g. tablets of 5 mg and 10 mg). Low strength bromocriptine tablets (e.g. 2.5 mg) used as a prolactin inhibitor are classified in G02CB - *Prolactin inhibitors*.

Cabergoline used in parkinsonism is classified in this group (e.g. tablets of 1 mg). Low strength cabergoline tablets (0.5 mg) used as a prolactin inhibitor are classified in G02CB.

Lisuride in high strength formulations (e.g. 0.2 mg tablets), which is also used in the treatment of Parkinsonism, are classified in G02CB while lisuride in low strength formulations (e.g. 25 mcg tablets) are classified in N02CA.

N04BD Monoamine oxidase B inhibitors

N04BX Other dopaminergic agents

This group comprises dopaminergic agents which cannot be classified in the preceding groups.

The combination of levodopa, decarboxylase inhibitor and COMT inhibitor is classified in N04BA - *Dopa and dopa derivatives*.

N05 PSYCHOLEPTICS

The group is divided into therapeutic subgroups:

N05A - *Antipsychotics*

N05B - *Anxiolytics*

N05C - *Hypnotics and sedatives*

N05A ANTIPSYCHOTICS

This group comprises drugs with antipsychotic actions (i.e. neuroleptics).

Reserpine is classified in C02 - *Antihypertensives*.

Antipsychotics in combination with antidepressants are classified in N06C - *Psycholeptics and psychoanaleptics in combination*.

The group is subdivided mainly according to chemical structure.

The DDDs are based on the treatment of psychosis. The substances in this group are sometimes used for other indications in much lower doses.

For depot injections, the DDDs are based on the average recommended doses divided by the dosing interval.

N05AA Phenothiazines with aliphatic side-chain

N05AB Phenothiazines with piperazine structure

N05AC Phenothiazines with piperidine structure

N05AD Butyrophenone derivatives

Parenteral formulations of droperidol are classified in N01AX, while oral formulations are classified in this group.

N05AE Indole derivatives

N05AF Thioxanthene derivatives

N05AG Diphenylbutylpiperidine derivatives

N05AH Diazepines, oxazepines, thiazepines and oxepines

N05AL Benzamides

N05AN *Lithium*

The DDD is based on the prophylaxis of mania or depression.

Antidepressants, see N06A.

N05AX *Other antipsychotics*

This group comprises antipsychotics which cannot be classified in the preceding groups.

N05B ANXIOLYTICS

This group comprises preparations used in the treatment of neuroses and psychosomatic disorders associated with anxiety and tension, e.g. benzodiazepines.

See also:

N05A - *Antipsychotics*

N05C - *Hypnotics and sedatives*

Usually the presence of an anxiolytic (or other psycholeptics) in combined preparations must be regarded as being of secondary importance and the preparations should be classified in the respective therapeutic groups (e.g. A03C - *Antispasmodics in combination with psycholeptics*, N02 - *Analgesics*).

Combined preparations used mainly for the treatment of anxiety are classified at separate 5th levels using the corresponding 50-series.

The group is subdivided according to chemical structure.

The DDDs are based on the treatment of anxiety.

N05BA *Benzodiazepine derivatives*

Benzodiazepines used mainly in the treatment of sleep disturbances are classified in N05C - *Hypnotics and sedatives*.

Benzodiazepines used mainly in the treatment of epilepsy are classified in N03 - *Antiepileptics*.

The parenteral DDD for chlordiazepoxide is higher than the oral DDD due to lower bioavailability for intramuscular injections.

N05BB Diphenylmethane derivatives

N05BC Carbamates

N05BD Dibenzo-bicyclo-octadiene derivatives

N05BE Azaspirodecanedione derivatives

N05BX Other anxiolytics

This group comprises anxiolytics which cannot be classified in the preceding groups.

N05C HYPNOTICS AND SEDATIVES

This group comprises preparations with mainly sedative or hypnotic actions.

See also:

N05A - *Antipsychotics*

N05B - *Anxiolytics*

R06A - *Antihistamines for systemic use*

Combined preparations are classified at separate 4th levels, N05CB and N05CX.

Regarding classification of combined preparations, see comments under N05B - *Anxiolytics*.

Combined preparations with barbiturates are mainly classified in A03 (mainly antispasmodic effect) or in N02 (mainly analgesic effect).

Combined preparations with barbiturates which remain in N05C are mainly "neurostabilizers".

The group is subdivided according to chemical structure.

The DDDs are based on use of the drugs as hypnotics.

N05CA Barbiturates, plain

This group comprises barbiturates used for insomnia.

Preparations used as premedication are also classified in this group.

Barbiturates used in general anesthesia are classified in N01A - *General anesthetics*.

Barbiturates used mainly in the treatment of epilepsy, e.g. phenobarbital, are classified in N03 - *Antiepileptics*.

Combined preparations are classified in N05CB, see comment under N05C.

N05CB Barbiturates, combinations

This group comprises combined preparations with mainly sedative action. Combinations with analgesics etc., see comments under N05C - *Hypnotics and sedatives*.

Tetrabamate is classified here.

N05CC Aldehydes and derivatives

N05CD Benzodiazepine derivatives

Benzodiazepine derivatives used mainly in sleeping disorders are classified in this group.

See also N05BA.

N05CE Piperidinedione derivatives

N05CF Benzodiazepine related drugs

N05CH Melatonin receptor agonists

N05CM Other hypnotics and sedatives

This group includes drugs, which cannot be classified in the preceding groups.

N05CX Hypnotics and sedatives in combination, excl. barbiturates

All combination products mainly used in sleeping disorders are classified in this group, except combinations with barbiturates, see N05CB.

N06 PSYCHOANALEPTICS

This group comprises antidepressants, psychostimulants, nootropics anti-dementia drugs and combinations with psycholeptics.

Antiobesity preparations are classified in A08 - *Antiobesity preparations, excl. diet products*.

N06A ANTIDEPRESSANTS

This group comprises preparations used in the treatment of endogenous and exogenous depressions.

The group is subdivided mainly according to mode of action. The various antidepressants have different modes of action, and the classification will not reflect the exact mode of action of the various antidepressants.

Lithium, see N05AN - *Lithium*

Combination with psycholeptics, see N06C.

The DDDs are based on treatment of moderately severe depressions.

N06AA Non-selective monoamine reuptake inhibitors

N06AB Selective serotonin reuptake inhibitors

N06AF Monoamine oxidase inhibitors, non-selective

N06AG Monoamine oxidase A inhibitors

N06AX Other antidepressants

This group includes antidepressants, which cannot be classified in the preceding groups.

**N06B PSYCHOSTIMULANTS, AGENTS USED FOR ADHD AND
NOOTROPICS**

Nootropics are classified in N06BX.

N06BA Centrally acting sympathomimetics

Amphetamine is classified in this group, see comment under A08AA - *Centrally acting antiobesity products*.

Since atomoxetine is approved for use both in children, adolescents and in adults, the DDD is based on the treatment of a 70 kg person. The majority of the users will, however, probably be under 18 years of age.

N06BC Xanthine derivatives

Caffeine in combination with respiratory stimulants is classified in R07AB.

N06BX Other psychostimulants and nootropics

This group comprises substances regarded as nootropics. Psychostimulants, which cannot be classified in the preceding groups, are also classified here.

Cyprodenate (deanol cyclohexylpropionate) is classified in N06BX04.

N06C PSYCHOLEPTICS AND PSYCHOANALEPTICS IN COMBINATION

Combinations of e.g. antidepressants and anxiolytics are classified in this group.

N06CA Antidepressants in combination with psycholeptics

Preparations are classified at 5th levels according to the antidepressant. At each level various psycholeptics may occur.

N06CB Psychostimulants in combination with psycholeptics

N06D ANTI-DEMENTIA DRUGS

N06DA Anticholinesterases

N06DX Other anti-dementia drugs

N07 OTHER NERVOUS SYSTEM DRUGS

This group comprises other nervous system drugs, which cannot be classified in the preceding 2nd levels in ATC group N.

N07A PARASYMPATHOMIMETICS

See also cholinergics used in glaucoma therapy, S01EB.

This group includes various drugs used for different indications. The DDDs are therefore established individually for each ATC 5th level.

N07AA Anticholinesterases

N07AB Choline esters

N07AX Other parasympathomimetics

N07B DRUGS USED IN ADDICTIVE DISORDERS

This group comprises drugs used for maintenance treatment of addictive disorders. Drugs used for detoxification are classified in V03A - *All other therapeutic products*.

N07BA *Drugs used in nicotine dependence*

Bupropion is classified in N06A - *Antidepressants*.

The DDD for chewing gum and lozenges is identical.

N07BB *Drugs used in alcohol dependence*

Naltrexone, which is also used in the treatment of opioid dependence, see N07BC, is classified in this group.

N07BC *Drugs used in opioid dependence*

Low strength formulations of buprenorphine (equal or less than 0.4 mg) are classified in N02AE. Naltrexone is classified in N07BB - *Drugs used in alcohol dependence*.

Combinations of buprenorphine and naloxone are classified here.

N07C ANTIVERTIGO PREPARATIONS

This group comprises agents mainly used in the treatment of vertigo.

See also:

A04A - *Antiemetics and antinauseants*

C04AX - *Other peripheral vasodilators*

N02C - *Antimigraine preparations*

N05A - *Antipsychotics*

R06A - *Antihistamines for systemic use*

The DDDs are based on treatment of vestibular symptoms.

N07CA Antivertigo preparations

Combinations of cinnarizine and diphenhydramine teoclate (dimenhydrinate) are classified here.

N07X OTHER NERVOUS SYSTEM DRUGS

N07XA Gangliosides and ganglioside derivatives

N07XX Other nervous system drugs

This group contains substances, which cannot be classified in the preceding groups.

P ANTIPARASITIC PRODUCTS, INSECTICIDES AND REPELLENTS

P01 ANTIPROTOZOALS

A Agents against amoebiasis and other protozoal diseases

B Antimalarials

C Agents against leishmaniasis and trypanosomiasis

P02 ANTHELMINTICS

B Antitrematodals

C Antinematodal agents

D Anticestodals

P03 ECTOPARASITICIDES, INCL. SCABICIDES, INSECTICIDES AND REPELLENTS

A Ectoparasiticides, incl. scabicides

B Insecticides and repellents

P ANTIPARASITIC PRODUCTS, INSECTICIDES AND REPELLENTS

The group is subdivided according to types of parasites.

P01 ANTIPROTOZOALS

P01A AGENTS AGAINST AMOEBIASIS AND OTHER PROTOZOAL DISEASES

This group comprises drugs mainly used for amoeba infections and other protozoal diseases such as giardiasis and trichomoniasis.

P01AA Hydroxyquinoline derivatives

All combined preparations containing clioquinol are classified in this group. Formulations of chlorquinaldol and clioquinol for dermatological use are classified in D08AH.

No DDDs are established in this group.

P01AB Nitroimidazole derivatives

Nitroimidazole derivatives used for amoebiasis, trichomoniasis and giardiasis are classified in this group. Formulations for vaginal administration are classified in G01AF. Parenteral formulations mainly used for treatment of anaerobic bacterial infections are classified in J01XD. Fixed combination packages for eradication of *Helicobacter pylori* are classified in A02BD.

The DDDs are based on the treatment of amoebiasis, giardiasis and trichomoniasis. The duration of the treatment periods is not taken into consideration.

P01AC Dichloroacetamide derivatives

This group comprises luminal amoebicides.

The DDDs in this group are based on treatment of luminal amoebiasis.

P01AR Arsenic compounds

This group comprises e.g. glycobiarsol. Combinations containing clioquinol are classified in P01AA.

P01AX Other agents against amoebiasis and other protozoal diseases

This group comprises agents, which cannot be classified in the preceding groups. Combinations with clioquinol are classified in P01AA.

P01B ANTIMALARIALS

This group comprises drugs mainly used for treatment and prophylaxis of malaria.

The DDDs are based on the treatment of malaria, except for proguanil, which is used for prophylaxis only. For some substances the DDDs are expressed as amount of base. These are indicated in the ATC index.

P01BA Aminoquinolines

Combinations with clioquinol are classified in P01AA. Combinations with glycobiarsol are classified in P01AR.

The DDDs are based on the average daily dose for the treatment period.

P01BB Biguanides

The DDD for proguanil is based on the daily dose given for prophylaxis of malaria. The DDD for *proguanil, combinations* is based on treatment of acute malaria, see list of DDDs for combination products www.whooc.no.

P01BC Methanolquinolines

Combined preparations with quinine and psycholeptics used for treatment of nocturnal cramps are classified in M09AA.

Combined preparations with quinine for symptomatic relief in cold conditions are classified in R05X.

Hydroquinine is classified in M09AA.

P01BD Diaminopyrimidines

The DDD for pyrimethamine is based on combination therapy with a sulphonamide for the treatment of malaria.

P01BE Artemisinin and derivatives, plain

The parenteral DDD for arthemether is based on monotherapy.

The DDDs for artemisinin derivatives are based on combination therapy with other antimalarials.

P01BF Artemisinin and derivatives, combinations

P01BX Other antimalarials

This group comprises agents, which cannot be classified in the preceding groups. Combinations of diphenhydramine and diethyltoluamide are classified at the plain level for diphenhydramine in D04AA.

The DDD for halofantrine is based on a one-day (12h) treatment.

P01C AGENTS AGAINST LEISHMANIASIS AND TRYPANOSOMIASIS

P01CA *Nitroimidazole derivatives*

Nitroimidazole derivatives used for trypanosomiasis are classified in this group. Other nitroimidazole derivatives, see P01AB.

The DDD for benznidazole is based on the treatment of trypanosomiasis.

P01CB *Antimony compounds*

The DDDs are expressed as pentavalent antimony (Sb^{5+}) used in the treatment of visceral leishmaniasis.

P01CC *Nitrofurans derivatives*

The DDDs are based on the treatment of trypanosomiasis.

P01CD *Arsenic compounds*

The DDDs are based on the treatment of trypanosomiasis.

P01CX *Other agents against leishmaniasis and trypanosomiasis*

This group comprises agents, which cannot be classified in the preceding groups.

The DDD for pentamidine isethionate is based on amount given per injection. The DDD for suramin sodium is based on the average daily dose for the treatment period.

P02 ANTHELMINTICS

The anthelmintics are subdivided according to the main type of worms (i.e. trematodes, nematodes and cestodes) causing the infections.

P02B ANTITREMATODALS

This group comprises drugs mainly used for trematode infections such as e.g. schistosomiasis. Niclosamide, which is also used in trematode infections, is classified in P02DA.

The DDDs are based on the treatment of schistosomiasis.

P02BA Quinoline derivatives and related substances

P02BB Organophosphorous compounds

Metrifonate is administered every second week. The DDD is the dose divided by the dosing interval.

P02BX Other antitrematodal agents

This group comprises agents, which cannot be classified in the preceding groups.

P02C ANTINEMATODAL AGENTS

This group comprises drugs mainly used for nematode infections.

The DDDs are based on the treatment of different nematode infections e.g. ascariasis (roundworm) and hookworm infections.

P02CA Benzimidazole derivatives

P02CB Piperazine and derivatives

E.g. diethylcarbamazine is classified in this group.

The DDD for diethylcarbamazine is based on the treatment of lymphatic filariasis.

P02CC Tetrahydropyrimidine derivatives

P02CE Imidazothiazole derivatives

P02CF Avermectines

P02CX Other antinematodals

This group comprises agents, which cannot be classified in the preceding groups.

P02D ANTICESTODALS

This group comprises drugs mainly used for cestode infections. Praziquantel and mebendazole which are also used in cestode infections, are classified in P02BA and P02CA respectively.

The DDDs are based on the treatment of cestode (tapeworm) infections.

P02DA Salicylic acid derivatives

P02DX Other anticestodals

This group comprises agents, which cannot be classified in the preceding groups.

P03 ECTOPARASITICIDES, INCL. SCABICIDES, INSECTICIDES AND REPELLENTS

No DDDs are assigned in this group. Substances classified in this group are for topical use and the consumption figures for these preparations could be expressed in e.g. grams of preparations regardless of strength.

P03A ECTOPARASITICIDES, INCL. SCABICIDES

This group comprises preparations used against scabies, lice and other ectoparasites.

P03AA Sulfur containing products

Combinations with e.g. benzyl benzoate are classified in this group.

Combinations with chlorine compounds, see P03AB.

P03AB Chlorine containing products

Combinations with sulfur compounds are classified in this group.

P03AC Pyrethrines, incl. synthetic compounds

This group comprises various pyrethrum products, including synthetic pyrethrinoids and combinations with e.g. piperonyl butoxide.

Combinations with malathion are classified here.

P03AX Other ectoparasiticides, incl. scabicides

Crotamiton preparations are classified in D04AX - *Other antipruritics*.

Combinations of benzyl benzoate and sulfur containing compounds are classified in P03AA.

Dimeticone used as antifatulent is classified in A03AX13 - *silicones*.

P03B INSECTICIDES AND REPELLENTS

P03BA Pyrethrines

P03BX Other insecticides and repellents

R RESPIRATORY SYSTEM

R01 NASAL PREPARATIONS

A Decongestants and other nasal preparations for topical use

B Nasal decongestants for systemic use

R02 THROAT PREPARATIONS

A Throat preparations

R03 DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES

A Adrenergics, inhalants

B Other drugs for obstructive airway diseases, inhalants

C Adrenergics for systemic use

D Other systemic drugs for obstructive airway diseases

R05 COUGH AND COLD PREPARATIONS

C Expectorants, excl. combinations with cough suppressants

D Cough suppressants, excl. combinations with expectorants

F Cough suppressants and expectorants, combinations

X Other cold combination preparations

R06 ANTIHISTAMINES FOR SYSTEMIC USE

A Antihistamines for systemic use

R07 OTHER RESPIRATORY SYSTEM PRODUCTS

A Other respiratory system products

R RESPIRATORY SYSTEM

Inhaled antiinfectives are classified in ATC group J - *Antiinfectives for systemic use*.

R01 NASAL PREPARATIONS

R01A DECONGESTANTS AND OTHER NASAL PREPARATIONS FOR TOPICAL USE

This group comprises preparations for local treatment in nasal congestion (e.g. sympathomimetics) or for prophylaxis and treatment of allergic rhinitis (e.g. corticosteroids, cromoglicate preparations). Most of the products are nasal drops, nasal sprays or nasal inhalants.

See also R01B - *Nasal decongestants for systemic use*, and R06 - *Antihistamines for systemic use*.

The DDDs are based on treatment of both nostrils.

R01AA Sympathomimetics, plain

Small amounts of antiseptics etc. are allowed at each 5th level.

Combinations with antibiotics, antihistamines, ipatropium bromide etc. are classified in R01AB, while combinations with corticosteroids are classified in R01AD.

The DDDs are based on the treatment of acute rhinitis.

R01AB Sympathomimetics, combinations excl. corticosteroids

Combinations with e.g. antibiotics, antihistamines and ipatropium bromide are classified in this group.

This group also includes preparations with two or more sympathomimetics. These combinations are classified in a ranking according to the ATC codes, e.g. substances classified in R01AB01 take precedence over substances classified in R01AB02 etc.

The DDDs are based on the treatment of rhinitis. DDDs are given in volume (i.e. ml). Most of the products classified in this group are combinations with antihistamines. So far, all these products are given a fixed DDD of 0.8 ml.

R01AC Antiallergic agents, excl. corticosteroids

Antihistamines, cromoglicate disodium and analogues are classified here.

The DDD of cromoglicic acid is based on the prophylaxis of rhinitis. The DDDs of the antihistamines are based on the maintenance treatment of rhinitis.

R01AD Corticosteroids

Combinations of corticosteroids and antiinfectives, sympathomimetics etc. should be classified in this group at separate 5th levels by using the 50-series.

Fluticasone propionate is classified in R01AD08.

The DDDs are mainly based on the starting dose in the treatment of rhinitis.

R01AX Other nasal preparations

This group comprises antiinfectives, antiseptics, mucolytics etc. which cannot be classified in the preceding groups.

ATC level R01AX10 is an old level where rather obsolete nasal preparations and sodium chloride nasal products are classified. The level R01AX30 is for nasal combination products which cannot be classified in the preceding groups.

Combinations of ipatropium bromide and xylometazoline are classified in R01AB.

The DDDs are based on the treatment of rhinitis.

R01B NASAL DECONGESTANTS FOR SYSTEMIC USE

This group comprises preparations for systemic use in vasomotoric or allergic rhinitis etc., excl. plain antihistamines (see R06).

Combinations with antihistamines are classified in this group.

The DDDs are based on the treatment of rhinitis.

R01BA *Sympathomimetics*

R02 THROAT PREPARATIONS

R02A THROAT PREPARATIONS

Throat preparations and mouth preparations are classified in the groups R02 and A01 according to assumed main therapeutic use. Preparations used in common minor infections of mouth and throat are classified in R02, while preparations used in gingivitis, stomatitis etc. are classified in A01 - *Stomatological preparations*.

Expectorants administered as tablets are classified in R05 - *Cough and cold preparations*.

The DDDs are based on the treatment of common minor infections of mouth and throat. For combination products, DDDs are given as fixed doses of 6 UD (6 tablets).

R02AA *Antiseptics*

See also A01AB - *Antiinfectives and antiseptics for local oral treatment*.
At each 5th level combinations with anesthetics are allowed.

The combination dichlorobenzyl alcohol and amyl-m-cresol is classified in R02AA03.

R02AB *Antibiotics*

See also A01AB - *Antiinfectives and antiseptics for local oral treatment*.

At each 5th level combinations with anesthetics and/or steroids are allowed.

Antibiotics for systemic use, see J01.

R02AD Anesthetics, local

This group comprises e.g. throat lozenges containing local anesthetics. Dental anesthetics for local application are classified in N01B - *Anesthetics, local*.

Combinations of anesthetics and antiseptics/antibiotics are classified in R02AA/R02AB respectively.

R02AX Other throat preparations

R03 DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES

R03A ADRENERGICS, INHALANTS

It is complicated to decide DDDs for the different dosage forms and even the different inhalation *devices* of the same dosage form. It has been shown that certain inhalation devices give a better deposition of the active ingredient in the lungs. This gives a better clinical effect, and therefore the active ingredients can be used in lower dosages. It has been decided not to take this aspect into consideration when assigning DDDs in this group, since the picture is very complex and satisfactory comparative documentation is not always available. Accordingly, only one DDD is assigned for one dosage form of a substance (e.g. powder inhalation).

For some substances, the labelling of the strength of identical inhalation products may differ between countries. In some countries, metered dose (measured as the amount of substance released from the inhaler with the mouthpiece removed) is used while in other countries delivered dose (measured as the amount of substance released from the inhaler with the mouthpiece in place) is used in the labelling. Delivered dose will usually be lower than metered dose. This is important to take into considerations when linking DDD information to the products in the different countries.

The DDDs for inhalation aerosol and inhalation powder of the same substance are in most cases given the same DDD value. The DDDs for inhalation solutions are, however, different from these and much higher, partly because less amount of the active ingredient will reach the target organ, and partly because this dosage form often is used in more severe and unresponsive asthma.

R03AA Alpha- and beta-adrenoreceptor agonists

The DDDs are based on the treatment of asthma.

R03AB Non-selective beta-adrenoreceptor agonists

The DDDs are based on the treatment of asthma.

R03AC Selective beta-2-adrenoreceptor agonists

The DDDs are mainly based on the treatment of asthma.

The DDDs for formoterol and salmeterol inhalation powders are based on metered dose, even though products containing these substances could be declared as delivered dose.

R03AH Combinations of adrenergics

See comments to R03AK.

R03AK Adrenergics and other drugs for obstructive airway diseases

All adrenergics for inhalation in combination with other drugs for obstructive airway diseases are classified in this group.

The preparations are classified at 5th levels according to the adrenergic component. At each 5th level different drugs for obstructive airway diseases may occur.

The DDDs for combination products are based on the maintenance treatment of severe asthma or COPD (Chronic Obstructive Pulmonary Disease). The assigned DDDs cannot always be compared with the DDDs assigned for plain preparations. See list of DDDs for combination products; www.whooc.no.

R03B OTHER DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES, INHALANTS

This group comprises all drugs for obstructive airway diseases for inhalation excl. adrenergics (R03A).

See comment under R03A.

R03BA *Glucocorticoids*

The DDDs are based on the starting dose in moderate to severe asthma.

R03BB *Anticholinergics*

Combinations with adrenergics are classified in R03AK.

The DDDs are based on the maintenance treatment of asthma.

The DDDs for tiotropium bromide are based on treatment of COPD (Chronic Obstructive Pulmonary Disease).

R03BC *Antiallergic agents, excl. corticosteroids*

The DDDs are based on the prophylaxis of asthma.

DDD for inhalation aerosol and inhalation powder differ in this group, due to differences in dosage recommendations for these dosage forms.

R03BX *Other drugs for obstructive airway diseases, inhalants*

R03C ADRENERGICS FOR SYSTEMIC USE

This group comprises adrenergics for systemic use indicated for e.g. bronchial asthma. Sympathomimetics used in the treatment of hypotension, see C01CA. Fenoterol infusion only intended for repression of labour is classified in G02CA. Combinations with xanthines are classified in R03DB. Combinations with other anti-asthmatics are classified in R03CK.

R03CA *Alpha- and beta-adrenoreceptor agonists*

Ephedrine injections are classified in C01CA.

R03CB *Non-selective beta-adrenoreceptor agonists*

Isoprenaline for systemic use is classified in this group only if bronchial asthma is the only indication for the preparation, otherwise in C01C - *Cardiac stimulants excl. cardiac glycosides*.

R03CC *Selective beta-2-adrenoreceptor agonists*

R03CK *Adrenergics and other drugs for obstructive airway diseases*

Combinations of adrenergics and other drugs for obstructive airway diseases (excl. xanthines, see R03DB) are classified here.

R03D OTHER SYSTEMIC DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES

Theophyllines are classified in this group. Other respiratory stimulants are classified in R07AB - *Respiratory stimulants*.

Corticosteroids for systemic use, see H02.

Sympathomimetics for systemic treatment of rhinitis, see R01BA.

This group comprises mainly the xanthines. The DDDs for these substances are based on treatment of obstructive lung diseases.

R03DA Xanthines

A number of preparations containing e.g. theophylline are classified in this group even if they do not have asthma as an indication.

Combinations of xanthines and other agents (except adrenergics, see R03DB - *Xanthines and adrenergics*) are classified at separate 5th levels using the corresponding 50-series (e.g. mucolytics).

R03DB Xanthines and adrenergics

All combinations of xanthines and adrenergics are classified in this group.

R03DC Leukotriene receptor antagonists

R03DX Other systemic drugs for obstructive airway diseases

This group comprises preparations, which cannot be classified in the preceding groups.

R05 COUGH AND COLD PREPARATIONS

This group comprises a large number of preparations, most of which are combined preparations.

Cold preparations containing therapeutic levels of antiinfectives should be classified in ATC group J - *Antiinfectives for systemic use*.

Cold preparations with therapeutic levels of analgesics/anti-inflammatory agents should be classified in the respective N02/M01 groups, at separate 5th levels by using the 50-series.

Cold preparations with both antiinfectives and analgesics should be classified in ATC group J - *Antiinfectives for systemic use*.

Cold preparations with minimal amounts of antiinfectives or analgesics are classified in R05X - *Other cold combination preparations*.

See also R01 - *Nasal preparations*, R02 - *Throat preparations*, and R03D - *Other systemic drugs for obstructive airway diseases*.

Fixed DDDs are assigned for combinations. These DDDs are based on an average dose regimen of three times daily, and dosages in the upper area of the recommended dose ranges are chosen. The strengths of the various components are not taken into consideration. E.g. 6 UD (= 30 ml) is the fixed DDD for products where the recommended dose is 5-10 ml.

R05C EXPECTORANTS, EXCL. COMBINATIONS WITH COUGH SUPPRESSANTS

This group comprises preparations with expectorants and mucolytics.

Combined preparations are classified at separate 5th levels using the code number 10. These may also contain bronchodilating agents, antihistamines etc.

Preparations, which contain small amounts of herbal extracts, menthol etc., are regarded as plain preparations.

R05CA *Expectorants*

All combined products of expectorants are classified in R05CA10.

R05CB *Mucolytics*

Mesna in i.v. formulations used for the prophylaxis of urothelial toxicity is classified in V03AF. Mesna used as a mucolytic agent (e.g. administered by a nebuliser) is classified here.

All combined products of mucolytics are classified in R05CB10. Combinations with xanthines are classified in R03DA.

Combinations with antiinflammatory agents are classified in M01.

For acetylcysteine, the DDD for inhalation solution is higher than for the oral formulation, due to differences in the dosages recommended.

R05D COUGH SUPPRESSANTS, EXCL. COMBINATIONS WITH EXPECTORANTS

Combined preparations are classified at separate 5th levels using the code number 20 (R05DA20 and R05DB20). These may also contain bronchodilating agents, antihistamines etc.

Combinations with expectorants, see R05F.

Combinations with xanthines, see R03DA.

Preparations, which contain small amounts of herbal extracts, menthol etc., are not regarded as combined preparations.

R05DA Opium alkaloids and derivatives

Plain codeine, also when used as an analgesic, is classified in this group.

All combined products of opium alkaloids and derivatives, are classified in R05DA20.

All dihydrocodeine products, also when used as cough suppressants, are classified in N02AA.

R05DB Other cough suppressants

All combined products of other cough suppressants are classified in R05DB20.

Levocloperastine is classified together with cloperastine in R05DB21.

R05F COUGH SUPPRESSANTS AND EXPECTORANTS, COMBINATIONS

In addition to cough suppressants and expectorants, the preparations may contain bronchodilating agents, antihistamines etc. Combinations, which contain respiratory stimulants, e.g. theophylline, should be classified in R03DA.

R05FA Opium derivatives and expectorants

R05FB Other cough suppressants and expectorants

R05X OTHER COLD COMBINATION PREPARATIONS

This group comprises cold preparations with various ingredients, which cannot be classified in the preceding groups. Combinations with therapeutic amounts of various ingredients (e.g. quinine as an antipyretic, antihistamines, ascorbic acid and caffeine) are classified in this group. Various remedies for symptomatic relief in cough and cold, e.g. inhalants with menthol, camphora, thymol etc. are also classified here.

R06 ANTIHISTAMINES FOR SYSTEMIC USE

R06A ANTIHISTAMINES FOR SYSTEMIC USE

This group comprises plain and combined antihistamine preparations for systemic use. Antihistamines used in motion sickness are classified in this group. Other preparations used in motion sickness, see A04 - *Antiemetics and antinauseants*.

See also N07C - *Antivertigo preparations*.

Combined preparations (incl. combinations with hydroxyzine) are classified at separate 5th levels using the corresponding 50-series.

Combinations of antihistamines are classified at a separate 4th level, R06AK.

Antihistamines are also included in combined preparations classified in other groups:

Combinations with analgesics - N02

Combinations with xanthines - R03DA

Combinations with expectorants - R05C

Combinations with nasal decongestants for systemic use - R01B

Combinations with cough suppressants - R05D

Allergen extracts, see V01.

The group is subdivided according to chemical structure.

For some of the substances, different dosage forms are given different DDDs, due to differences in bioavailability.

R06AA Aminoalkyl ethers

Combinations with codeine are classified in N02AA.

Combinations of cinnarizine and diphenhydramine teoclate (dimenhydrinate) are classified in N07CA - *Antivertigo preparations*.

Different DDDs are established for the two salts of diphenhydramine (ATC code R06AA02): -chloride and -teoclate (dimenhydrinate).

R06AB Substituted alkylamines

R06AC Substituted ethylene diamines

R06AD Phenothiazine derivatives

R06AE Piperazine derivatives

Cinnarizine and flunarizine are classified in N07C - *Antivertigo preparations*.

R06AK Combinations of antihistamines

R06AX Other antihistamines for systemic use

R07 OTHER RESPIRATORY SYSTEM PRODUCTS

R07A OTHER RESPIRATORY SYSTEM PRODUCTS

This group comprises lung surfactants and respiratory stimulants. Caffeine is classified in N06B - *Psychostimulants, agents used for ADHD and nootropics*. See also comments under R07AB - *Respiratory stimulants*.

R07AA Lung surfactants

This group comprises surface-tension lowering agents used in respiratory distress syndrome. Combinations of different lung surfactants are classified in R07AA30, e.g. sinapultide in combination with other lung surfactants are classified here.

The DDDs of colfosceril palmitate and natural phospholipids are based on the treatment of respiratory distress syndrome in neonates, and correspond to the treatment of children weighing 1.6 kg.

R07AB Respiratory stimulants

Centrally acting respiratory stimulants mainly used for asthma and similar respiratory diseases (e.g. theophylline) are classified in R03D. Other respiratory stimulants are classified here. This group includes plain and combined preparations.

Combinations with respiratory stimulants and caffeine are classified in this group. Plain caffeine preparations are classified in N06B *Psychostimulants, agents used for ADHD and nootropics*.

This group includes various drugs used on different indications. The DDDs are therefore established individually for each ATC 5th level.

R07AX Other respiratory system products

This group comprises preparations used for respiratory disorders, which cannot be classified in the preceding groups.

Nitric oxide is classified here, other medical gases, see V03AN.

S SENSORY ORGANS

S01 OPTHALMOLOGICALS

- A Antiinfectives*
- B Antiinflammatory agents*
- C Antiinflammatory agents and antiinfectives in combination*
- E Antiglaucoma preparations and miotics*
- F Mydriatics and cycloplegics*
- G Decongestants and antiallergics*
- H Local anesthetics*
- J Diagnostic agents*
- K Surgical aids*
- X Other ophthalmologicals*

S02 OTOLOGICALS

- A Antiinfectives*
- B Corticosteroids*
- C Corticosteroids and antiinfectives in combination*
- D Other otologicals*

S03 OPTHALMOLOGICAL AND OTOLOGICAL PREPARATIONS

- A Antiinfectives*
- B Corticosteroids*
- C Corticosteroids and antiinfectives in combination*
- D Other ophthalmological and otological preparations*

S **SENSORY ORGANS**

A formulation approved both for use in the eye/ear is classified in S03, while formulations only licensed for use in the eye or the ear are classified in S01 and S02, respectively.

S01 **OPHTHALMOLOGICALS**

Small amounts of antiseptics in eye preparations do not influence the classification, e.g. benzalconium.

See also S03 - *Ophthalmological and otological preparations*.

DDD's have been assigned for antiglaucoma preparations only.

S01A **ANTIINFECTIVES**

This group comprises plain and combined antiinfective preparations for ophthalmological use.

Combinations with corticosteroids are classified in S01CA - *Corticosteroids and antiinfectives in combination*.

S01AA *Antibiotics*

Combinations of different antibiotics (incl. sulfonamides) are classified at a separate 5th level: S01AA30.

Combinations with other drugs (e.g. sympathomimetics) are classified at a separate 5th level: S01AA20.

Combinations with antiinflammatory agents are classified in group S01C.

S01AB *Sulfonamides*

Combinations with antibiotics are classified in S01AA.

S01AD *Antivirals*

S01AX Other antiinfectives

This group comprises antiinfective preparations for ophthalmological use, which cannot be classified in the preceding groups. Products containing boric acid, also in low strengths, are classified in this group. Preparations containing benzalconium as the only active substance are classified here, on the 4th level.

S01B ANTIINFLAMMATORY AGENTS

This group comprises all eye preparations with non-steroidal antiinflammatory agents and corticosteroids, plain and combinations. Combinations with antiinfectives are classified in S01C - *Antiinflammatory agents and antiinfectives in combination*.

S01BA Corticosteroids, plain

S01BB Corticosteroids and mydriatics in combination

Combinations, which in addition contain anticholinergics, are classified here.

Combinations, which in addition contain antiinfectives, are classified in S01CB - *Corticosteroids/antiinfectives/mydriatics in combination*.

S01BC Antiinflammatory agents, non-steroids

S01C ANTIINFLAMMATORY AGENTS AND ANTIINFECTIVES IN COMBINATION

This group comprises all eye preparations, which contain corticosteroids or non-steroidal antiinflammatory agents and antiinfectives. Preparations may also contain additional drugs.

S01CA Corticosteroids and antiinfectives in combination

The preparations are classified according to the corticosteroid. Different antiinfectives may occur at each 5th level.

S01CB Corticosteroids/antiinfectives/mydriatics in combination

This group is built up as S01CA.

S01CC Antiinflammatory agents, non-steroids and antiinfectives in combination

S01E ANTIGLAUCOMA PREPARATIONS AND MIOTICS

This group comprises preparations for local and systemic treatment of glaucoma.

Drugs used for producing miosis are classified in this group, even if the main indication is not glaucoma.

The DDDs are based on single dose (or single package) and administration frequencies. A single dose is defined as two eye drops (one in each eye) corresponding to 0.1 ml. For eye drops administered once daily the DDD is 0.1 ml, for eye drops administered twice daily the DDD is 0.2 ml, etc. For single use packages one dose is the volume of one package. This also applies for combinations. In eye ointments one dose corresponds to about 10 mm (20 mg) per eye thus corresponding to 40 mg for both eyes.

S01EA Sympathomimetics in glaucoma therapy

Preparations containing parasympathomimetics in combination with epinephrine, are classified in S01EB.

S01EB Parasympathomimetics

Combinations with beta blocking agents are classified in S01ED.

The DDD for pilocarpine lamellas has been obtained by dividing two lamellas by seven days (the recommended dose is 1 lamella/eye/week).

S01EC Carbonic anhydrase inhibitors

The DDDs are based on the average recommended doses in the treatment of chronic glaucoma.

S01ED Beta blocking agents

Combinations of beta blocking agents and other drugs, e.g. pilocarpine, are classified in this group, at separate 5th levels using the corresponding 50-series.

S01EE Prostaglandin analogues

Combinations with beta blocking agents are classified in S01ED.

S01EX Other antiglaucoma preparations

S01F MYDRIATICS AND CYCLOPLEGICS

S01FA Anticholinergics

Combinations with sympathomimetics are classified in this group.

Combinations with corticosteroids are classified in S01BB.

S01FB Sympathomimetics excl. antiglaucoma preparations

Phenylephrine in high strength is classified in this group, see also S01GA.

Sympathomimetics used in glaucoma therapy, see S01EA.

S01G DECONGESTANTS AND ANTIALLERGICS

This group comprises drugs used to treat symptoms of e.g. allergy.

S01GA Sympathomimetics used as decongestants

This group comprises sympathomimetics used as decongestants, plain and in combination. E.g. low strength phenylephrine in combination with other drugs is classified in this group. See also S01FB.

S01GX Other antiallergics

Combinations of cromoglicic acid and antihistamines are classified in S01GX51.

S01H LOCAL ANESTHETICS

This group comprises topical drugs used as local anesthetics in the eye.

Local anesthetics for other indications are classified in N01B - *Anesthetics, local*. Other exceptions, see comments to N01B.

Combinations of local anesthetics and diagnostic agents, e.g. fluorescein, are classified in S01J.

S01HA *Local anesthetics*

S01J DIAGNOSTIC AGENTS

This group comprises topical drugs used for diagnosing diseases in the eye. Mydriatics and cycloplegics used as diagnostic aids are classified in S01F.

Diagnostic agents for systemic use for ophthalmological diagnoses, e.g. fluorescein injection, are classified in V04CX - *Other diagnostic agents*.

S01JA *Colouring agents*

S01JX *Other ophthalmological diagnostic agents*

S01K SURGICAL AIDS

This group comprises drugs used in ophthalmological surgery.

Miotics are classified in S01E - *Antiglaucoma preparations and miotics*.

Mydriatics and cycloplegics are classified in S01F.

S01KA *Viscoelastic substances*

Hyaluronic acid injection used during surgical procedures on the eye (e.g. 4-20 mg/ampoule) is classified in this group. Hyaluronic acid injection for intra-articular administration (e.g. 2.5 mg/ampoule) used in the treatment of arthritis is classified in M09A - *Other drugs for disorders of the musculo-skeletal system*.

Hypromellose is classified in this group. Hypromellose used as artificial tears is, however, classified in S01XA20.

S01KX Other surgical aids

Preparations containing e.g. enzymes (chymotrypsin) for use in eye surgery, are classified in this group.

S01L OCULAR VASCULAR DISORDER AGENTS

S01LA Antineovascularisation agents

S01X OTHER OPHTHALMOLOGICALS

This group comprises topical products, which cannot be classified in the preceding groups e.g. artificial tears, products for use with contact lenses, drugs against cataract etc.

All products containing boric acid are classified in S01AX - *Other antiinfectives*.

S01XA Other ophthalmologicals

Hypromellose is classified in S01XA20, if it is used as artificial tears. See also S01KA.

S02 OTOLOGICALS

Small amounts of antiseptics in otological preparations do not influence the classification, e.g. benzalconium.

See also S03 - *Ophthalmological and otological preparations*.

No DDDs are assigned in this group.

S02A ANTIINFECTIVES

This group comprises plain and combined antiinfective preparations for otological use.

Combined preparations are classified at a separate 5th level - S02AA30 - *antiinfectives, combinations*. This level includes combinations of different antiinfectives and combinations of antiinfectives/other substances.

Combinations with corticosteroids are classified in S02C - *Corticosteroids and antiinfectives in combination*.

S02AA *Antiinfectives*

Ciprofloxacin, declared as ear drops, is classified here.

S02B CORTICOSTEROIDS

This group comprises all otological preparations with corticosteroids, plain and combinations, except combinations with antiinfectives. These are classified in S02C - *Corticosteroids and antiinfectives in combination*.

S02BA *Corticosteroids*

S02C CORTICOSTEROIDS AND ANTIINFECTIVES IN COMBINATION

This group comprises all otological preparations, which contain corticosteroids and antiinfectives. Preparations may also contain additional drugs.

The preparations are classified at separate 5th levels according to the corticosteroid.

S02CA *Corticosteroids and antiinfectives in combination*

S02D OTHER OTOLOGICALS

This group comprises ear preparations, which cannot be classified in the preceding groups.

S02DA Analgesics and anesthetics

This group comprises e.g. preparations with analgesics and/or local anesthetics.

S02DC Indifferent preparations

This group comprises e.g. oil-preparations used to remove ear wax.

S03 OPHTHALMOLOGICAL AND OTOLOGICAL PREPARATIONS

This group comprises preparations which can be used in both eye and ear.

Small amounts of antiseptics (e.g. benzalconium) in eye/ear preparations do not influence the classification.

No DDDs are assigned in this group.

S03A ANTIINFECTIVES

S03AA Antiinfectives

This group comprises plain and combined antiinfective preparations for use in eye/ear.

Combined preparations are classified at a separate 5th level, S03AA30 - *antiinfectives, combinations*. This level includes combinations of different antiinfectives and combinations of antiinfectives and other substances.

Combinations with corticosteroids are classified in S03C - *Corticosteroids and antiinfectives in combination*.

S03B CORTICOSTEROIDS

This group comprises all eye/ear preparations with corticosteroids, plain and combinations, except combinations with antiinfectives. These are classified in S03C - *Corticosteroids and antiinfectives in combination*.

S03BA Corticosteroids

S03C CORTICOSTEROIDS AND ANTIINFECTIVES IN COMBINATION

This group comprises all eye/ear preparations which contain corticosteroids and antiinfectives. Preparations may also contain additional drugs.

The preparations are classified according to the corticosteroid.

S03CA Corticosteroids and antiinfectives in combination

S03D OTHER OPHTHALMOLOGICAL AND OTOLOGICAL PREPARATIONS

This group comprises eye/ear preparations, which cannot be classified in the preceding groups.

V VARIOUS

V01 ALLERGENS

A Allergens

V03 ALL OTHER THERAPEUTIC PRODUCTS

A All other therapeutic products

V04 DIAGNOSTIC AGENTS

B Urine tests

C Other diagnostic agents

V06 GENERAL NUTRIENTS

A Diet formulations for treatment of obesity

B Protein supplements

C Infant formulas

D Other nutrients

V07 ALL OTHER NON-THERAPEUTIC PRODUCTS

A All other non-therapeutic products

V08 CONTRAST MEDIA

A X-ray contrast media, iodinated

B X-ray contrast media, non-iodinated

C Magnetic resonance imaging contrast media

D Ultrasound contrast media

V09 DIAGNOSTIC RADIOPHARMACEUTICALS

A Central nervous system

B Skeleton

C Renal system

D Hepatic and reticulo endothelial system

E Respiratory system

F Thyroid

G Cardiovascular system

H Inflammation and infection detection

I Tumour detection

X Other diagnostic radiopharmaceuticals

V10 *THERAPEUTIC RADIOPHARMACEUTICALS*

A Antiinflammatory agents

B Pain palliation (bone seeking agents)

X Other therapeutic radiopharmaceuticals

V20 *SURGICAL DRESSINGS*

V VARIOUS

This group comprises many different types of drugs, and assigning DDDs are difficult. Very few DDDs are assigned in this group.

V01 ALLERGENS

V01A ALLERGENS

V01AA *Allergen extracts*

This group comprises preparations mainly used in hyposensitisation. Preparations for diagnostic use, e.g. prick and scratch tests, are classified in V04CL.

This group is divided according to type of allergen, e.g. grass pollen, tree pollen, fungi etc. *Artemisia vulgaris* allergens are classified in V01AA10 - flowers.

Oral and parenteral pharmaceutical forms are classified in the same ATC 5th level.

V03 ALL OTHER THERAPEUTIC PRODUCTS

V03A ALL OTHER THERAPEUTIC PRODUCTS

V03AB *Antidotes*

Sugammadex indicated for reversal of neuromuscular blockade induced by rocuronium or vecuronium is classified here.

Hydroxocobalamin is also classified in B03BA.

Medicinal charcoal is classified in A07BA.

Atropine is classified in A03BA.

Penicillamine, which is also used in copper poisoning, is classified in M01CC.

Silibinin, which is also used in amanita poisoning, is classified in A05BA at the same 5th level as silymarin.

Anticholinesterases, which are used as curare antidotes, are classified in N07AA.

Clonidine low strength tablets (e.g. 25 mcg) are classified in N02CX, even if the indication also may be “opioid withdrawal symptoms”. Both DL-methionine and L-methionine are included in the ATC 5th level V03AB26 - *methionine*.

Naltrexone is classified in N07BB - *Drugs used in alcohol dependence*.

Combinations of oxycodone and naloxone are classified in N02AA - *Natural opium alkaloids*.

Combinations of buprenorphine and naloxone are classified in N07BC - *Drugs used in opioid dependence*.

V03AC *Iron chelating agents*

V03AE *Drugs for treatment of hyperkalemia and hyperphosphatemia*

Plain calcium products also used in hyperphosphatemia are classified in A12AA.

The DDD for lanthanum carbonate is expressed as lanthanum and is equivalent to 4.3 g lanthanum carbonate.

V03AF *Detoxifying agents for antineoplastic treatment*

Mesna in i.v. formulations used for the prophylaxis of urothelial toxicity are classified in this group. Mesna used as a mucolytic agent (e.g. administered by a nebuliser) is classified in R05CB.

Rasburicase is classified here, other agents (e.g. febuxostat) for treatment of hyperuricaemia, see M04AA.

Glutathione is classified in V03AB - *Antidotes*.

The DDDs for calcium folinate, calcium levofolate, sodium folinate and sodium levofolate are based on the combined treatment with high doses of methotrexate.

The DDD for amifostine is based on the use as an adjunct in antineoplastic therapy.

V03AG Drugs for treatment of hypercalcemia

Sodium cellulose phosphate is classified here.
See also M05 - *Drugs for treatment of bone diseases*.

V03AH Drugs for treatment of hypoglycemia

Oral preparations containing diazoxide for treatment of hypoglycemia, are classified in this group, while parenteral preparations used for treatment of hypertension, are classified in C02DA.

V03AK Tissue adhesives

Human fibrinogen for systemic use is classified in B02BB01.

Fibrin sealants providing hemostasis at the site of application should be classified in B02BC.

V03AM Drugs for embolisation

V03AN Medical gases

Nitric oxide used in respiratory conditions is classified in R07AX.

V03AX Other therapeutic products

This group comprises agents, which cannot be classified in the preceding groups.

V03AZ Nerve depressants

V04 DIAGNOSTIC AGENTS

V04B URINE TESTS

V04C OTHER DIAGNOSTIC AGENTS

V04CA Tests for diabetes

V04CB Tests for fat absorption

V04CC Tests for bile duct patency

Pancreozymin is classified in V04CK.

V04CD Tests for pituitary function

See also V04CM - *Tests for fertility disturbances.*

V04CE Tests for liver functional capacity

V04CF Tuberculosis diagnostics

V04CG Tests for gastric secretion

V04CH Tests for renal function

V04CJ Tests for thyreoidea function

Thyrotropin alfa is classified in V04CJ01 - thyrotropin.

V04CK Tests for pancreatic function

V04CL Tests for allergic diseases

See also V01.

V04CM Tests for fertility disturbances

V04CX Other diagnostic agents

V06 GENERAL NUTRIENTS

This group comprises nutrients for oral use, incl. preparations used in feeding with stomach tube. Solutions for parenteral nutrition are classified in B05BA.

V06A DIET FORMULATIONS FOR TREATMENT OF OBESITY

See also A08 - *Antiobesity preparations, excl. diet products.*

V06AA Low-energy diets

V06B PROTEIN SUPPLEMENTS

V06C INFANT FORMULAS

This group comprises preparations used in metabolic disorders. Milk substitutes are classified V06DF.

V06CA Nutrients without phenylalanine

V06D OTHER NUTRIENTS

This group comprises a major part of the general nutrients.

V06DA Carbohydrates/proteins/minerals/vitamins, combinations

V06DB Fat/carbohydrates/proteins/minerals/vitamins, combinations

V06DC Carbohydrates

V06DD Amino acids, incl. combinations with polypeptides

V06DE Amino acids/carbohydrates/minerals/vitamins, combinations

V06DF Milk substitutes

This group comprises milk substitutes used in milk allergy.

V06DX Other combinations of nutrients

V07 ALL OTHER NON-THERAPEUTIC PRODUCTS

V07A ALL OTHER NON-THERAPEUTIC PRODUCTS

This group comprises e.g. solvents, diluents and solutions for blood transfusion products. Auxiliary products for performing medical examinations, e.g. plain exploration creams and lubricants, are also classified in this group.

V07AA Plasters

Non-medicated adhesive plasters, surgical tapes etc. are classified in this group whereas liquid plasters are classified in D02AD.

Medicated dressings are classified in D09.

V07AB Solvents and diluting agents, incl. irrigating solutions

This group comprises sterile water preparations and solvents for diluting or dissolving active substances, e.g. allergen extracts.

Storage solutions for the preservation of organs are also classified here.

V07AC Blood transfusion, auxiliary products

Citric acid/citrate/dextrose (ACD) solutions and similar products are classified in this group.

V07AD Blood tests, auxiliary products

Solutions used as diluents or transport media for blood samples are classified in this group.

V07AN Incontinence equipment

V07AR Sensitivity tests, discs and tablets

E.g. antibiotic discs may be classified in this group.

V07AS *Stomi equipment*

V07AT *Cosmetics*

V07AV *Technical disinfectants*

V07AX *Washing agents etc.*

V07AY *Other non-therapeutic auxiliary products*

Exploration creams and lubricants are classified in this group. Creams, which contain antiseptics, are classified in D08 - *Antiseptics and disinfectants*.

Preparations used as negative contrast media in double-contrast radiography only, containing e.g. bicarbonates or hypromellose, are classified in this group.

V07AZ *Chemicals and reagents for analysis*

V08 CONTRAST MEDIA

This group comprises X-ray, MRI and Ultrasound contrast media. The X-ray contrast media are subdivided into iodinated and non-iodinated compounds, and are further classified according to water solubility, osmolarity and nephrotropic/hepatotropic properties. High osmolar substances correspond mainly to ionic substances, except from ioxaglic acid, which is classified together with the non-ionic substances. MRI contrast media are subdivided according to magnetic properties.

V08A X-RAY CONTRAST MEDIA, IODINATED

V08AA *Watersoluble, nephrotropic, high osmolar X-ray contrast media*

V08AB *Watersoluble, nephrotropic, low osmolar X-ray contrast media*

V08AC *Watersoluble, hepatotropic X-ray contrast media*

V08AD *Non-watersoluble X-ray contrast media*

V08B X-RAY CONTRAST MEDIA, NON-IODINATED

V08BA *Barium sulfate containing X-ray contrast media*

V08C MAGNETIC RESONANCE IMAGING CONTRAST MEDIA

V08CA *Paramagnetic contrast media*

V08CB *Superparamagnetic contrast media*

V08CX *Other magnetic resonance imaging contrast media*

V08D ULTRASOUND CONTRAST MEDIA

V08DA *Ultrasound contrast media*

The microspheres may contain various ingredients. E.g. perflutren suspension in microspheres of phospholipids is classified in V08DA04.

Perflenapent covers structural isomers of dodecafluoropentane i.e. perflisopent.

V09 **DIAGNOSTIC RADIOPHARMACEUTICALS**

An expert group consisting of Dik Blok (the Netherlands), Per Oscar Bremer (Norway) and Trygve Bringhammar (Sweden) is responsible for the ATC classification of radiopharmaceuticals in V09 and V10. The group has also prepared the guidelines for classification of these products.

Radiopharmaceuticals for diagnostic use are classified in this group, while radiopharmaceuticals for therapeutic use are classified in V10. In general, the 3rd level are subdivided according to site of action or organ system, the 4th level according to radionuclide and the 5th level specifies the chemical substance. The ATC 5th level defines the actual form essential in nuclear medicine procedures, which includes radionuclide and carrier molecule. Therefore, products on the market, that can often be regarded as intermediate products rather than ready-to-use radiopharmaceuticals, can be given more than one (5th level) ATC code, e.g. Technetium (^{99m}Tc) exametazime (V09AA01) and technetium

(^{99m}Tc) exametazime labelled cells (V09HA02).

ATC codes are not assigned for radionuclide precursors which are used only in the radiolabelling of another substance prior to administration.

No DDDs have been assigned for radiopharmaceuticals.

V09A CENTRAL NERVOUS SYSTEM

This group comprises preparations used in CNS investigations in diagnostic nuclear medicine.

V09AA Technetium (^{99m}Tc) compounds

V09AB Iodine (^{123}I) compounds

V09AX Other central nervous system diagnostic radiopharmaceuticals

V09B SKELETON

This group comprises preparations used in bone imaging. Radiopharmaceuticals used for the investigation of bone marrow are classified in V09D - *Hepatic and reticulo endothelial system*.

V09BA Technetium (^{99m}Tc) compounds

This group comprises various technetium bisphosphonates and pyrophosphate.

V09C RENAL SYSTEM

This group comprises preparations used for the visualisation of kidneys and urinary tract and preparations for functional studies of the renal system.

V09CA Technetium (^{99m}Tc) compounds

This group comprises technetium compounds given intravenously. Technetium compounds used in aerosols for inhalation are classified in

V09E - *Respiratory system.*

Technetium-succimer prepared as 'pentavalent' is classified in V09I - *Tumour detection.*

V09CX *Other renal system diagnostic radiopharmaceuticals*

V09D HEPATIC AND RETICULO ENDOTHELIAL SYSTEM

This group comprises radiopharmaceuticals used for the imaging of liver, gall bladder, lymphatic system and bone marrow.

V09DA *Technetium (^{99m}Tc) compounds*

This group contains technetium iminodiacetic acid derivatives for cholescintigraphy.

V09DB *Technetium (^{99m}Tc), particles and colloids*

This group contains technetium colloidal and particle containing preparations for the scintigraphy of liver, spleen, lymphatic system and bone marrow. Also orally administered preparations used for gastrointestinal tract imaging (gastric emptying, reflux etc.) are classified in this group.

Preparations containing larger particles that are used for lung perfusion studies are classified in V09E - *Respiratory system.* Denatured labelled erythrocytes for spleen scintigraphy are classified in V09G - *Cardiovascular system.*

V09DX *Other hepatic and reticulo endothelial system diagnostic radiopharmaceuticals*

V09E RESPIRATORY SYSTEM

This group comprises radiopharmaceuticals for the lung ventilation and lung perfusion studies.

V09EA *Technetium (^{99m}Tc), inhalants*

Technetium preparations for inhalation are classified in this group. Preparations with other indications when given intravenously are

classified according to such indications, e.g. technetium-pentetate is classified in V09C - *Renal system*.

V09EB *Technetium (^{99m}Tc), particles for injection*

Preparations containing smaller particles or colloids that are used for RES function are classified in V09D - *Hepatic and reticulo endothelial system*.

V09EX *Other respiratory system diagnostic radiopharmaceuticals*

V09F THYROID

This group comprises radiopharmaceuticals used for thyroid imaging. Thalliumchloride and technetium-sestamibi used for parathyroid imaging are classified in V09G - *Cardiovascular system*.

V09FX *Various thyroid diagnostic radiopharmaceuticals*

Technetium-pertechnetate used for the scintigraphy of salivary glands and Meckels diverticulum is classified in this group. Technetium-pentavalent succimer used in medullary thyroid carcinoma is classified in V09I - *Tumour detection*. Sodium iodide (¹³¹I) in low dose is classified here. Sodium iodide (¹³¹I) in high dose for therapy is classified in V10X - *Other therapeutic radiopharmaceuticals*.

V09G CARDIOVASCULAR SYSTEM

This group comprises radiopharmaceuticals for myocardial scintigraphy, ejection fraction measurements, and vascular disorders.

V09GA *Technetium (^{99m}Tc) compounds*

Labelled cells (erythrocytes) for the investigation of cardiovascular function are classified in this group. No subdivision is made for in vitro or in vivo labelling. Pertechnetate for thyroid imaging is classified in V09F - *Thyroid*.

V09GB *Iodine (¹²⁵I) compounds*

V09GX *Other cardiovascular system diagnostic radiopharmaceuticals*

V09H INFLAMMATION AND INFECTION DETECTION

This group comprises agents for the detection of inflammation and infection. Labelled blood cells are classified in this group. Agents that are used for the labelling of these cells can also be classified elsewhere, e.g. technetium-exametazime is classified in V09A -*Central Nervous System*. No subdivision is made for the type of labelled cells (erythrocytes, granulocytes or autologous etc.).

V09HA *Technetium (^{99m}Tc) compounds*

V09HB *Indium (^{111}In) compounds*

V09HX *Other diagnostic radiopharmaceuticals for inflammation and infection detection*

V09I TUMOUR DETECTION

This group comprises monoclonal antibodies and other compounds used for tumour detection.

V09IA *Technetium (^{99m}Tc) compounds*

V09IB *Indium (^{111}In) compounds*

V09IX *Other diagnostic radiopharmaceuticals for tumour detection*

Gallium-citrate used for non-specific tumour localisation is classified in V09H - *Inflammation and infection detection*. Thallium-chloride used for tumour detection is classified in V09G -*Cardiovascular system*. Iobenguane (^{131}I) in low dose is classified here while high dose for therapy is classified in V10X -*Other therapeutic radiopharmaceuticals*.

V09X OTHER DIAGNOSTIC RADIOPHARMACEUTICALS

This group contains various diagnostic radiopharmaceuticals which cannot be classified in the preceding groups.

V09XA *Iodine (^{131}I) compounds*

V09XX *Various diagnostic radiopharmaceuticals*

V10 THERAPEUTIC RADIOPHARMACEUTICALS

Radiopharmaceuticals for therapeutic use are classified in this group, while radiopharmaceuticals for diagnostic use are classified in V09 - *Diagnostic radiopharmaceuticals*.

See comments to V09.

V10A ANTIINFLAMMATORY AGENTS

This group comprises radiopharmaceuticals for the therapy of inflammatory processes.

V10AA *Yttrium (⁹⁰Y) compounds*

In this group yttrium colloidal preparations used for radiation synovectomy are classified.

V10AX *Other antiinflammatory therapeutic radiopharmaceuticals*

This group comprises non-yttrium particulate radiopharmaceuticals for radiation synovectomy and intracavitary instillation.

V10B PAIN PALLIATION (BONE SEEKING AGENTS)

This group comprises therapeutic radiopharmaceuticals used for pain palliation in bone malignancies.

V10BX *Various pain palliation radiopharmaceuticals*

V10X OTHER THERAPEUTIC RADIOPHARMACEUTICALS

This group contains various therapeutic radiopharmaceuticals which cannot be classified in the preceding groups.

V10XA *Iodine (¹³¹I) compounds*

Sodium iodide (¹³¹I) in low dose for diagnostic nuclear medicine is classified in V09F - *Thyroid*.

Iobenguane (^{131}I) in low dose for diagnostic nuclear medicine is classified in V09I - *Tumour detection*.

V10XX *Various therapeutic radiopharmaceuticals*

V20 SURGICAL DRESSINGS

A detailed classification of surgical dressings is prepared and maintained by the Ministry of Defence in the UK.

List of terms:

AC-system	Anatomical Classification developed by the EphMRA (page 21).
ATC classification	Anatomical Therapeutic Chemical classification system (page 10, 15).
ATC herbal classification	ATC classification for herbal remedies (page 46).
ATCvet classification	ATC classification for veterinary products (page 46).
ATC levels	The ATC system is divided in 5 different levels. 1st level: 14 anatomical groups 2nd level: Pharmacological/therapeutic/ subgroup 3rd and 4th level: Chemical/pharmacological/therapeutic subgroups 5th level: Chemical substance (page 15).
Average adult dose	The dose used for the main indication which reflects the ATC code. When referred to body weight, an adult is considered to be a person of 70 kg. The DDDs are as a main rule based on the average adult dose (page 23).
BAN	British Approved Name (page 15).
5th level codes 20 and 30	5th level codes used for combined preparations containing two or more active ingredients belonging to the same 4th level. (e.g. page 19).
5th level codes - 50-series	Combination products containing two or more active components not belonging to the same 4th level are classified by using 50- series. (e.g. page 19).
5th level codes - 70 series	Combination products containing psycholeptic drugs, which are not classified under N05 or N06 are classified at separate 5th levels using the 70-series corresponding to the ATC-classification of the main component. (e.g. page 19).
Combination products	Products containing two or more active ingredients (page 19).
DDD	Defined Daily Dose - a technical unit of measurement defined as the assumed average maintenance dose per day for a drug used for its main indication in adults (page 22).
DDD/1000 inhabitants/day	Data presented as such provide a rough estimate of the proportion of the population within a defined area treated daily with certain drugs (page 34).

DDDs per 100 bed days	Applied when in-hospital drug use is considered. E.g. 100 DDD per 100 bed days indicates that for instance 20 persons get a certain treatment for 5 days (page 34).
DDDs per inhabitant per year	Often used for antiinfectives or other drugs normally used in short periods. E.g. 5 DDDs/inhabitant/year indicate that every inhabitant on average is treated with a 5 days course a year (page 34).
Double medication	Simultaneous use of two preparations containing the same chemical substance (the same 5th level) (page 36).
DURG	Drug Utilization Research Group (page 10).
EphMRA	European Pharmaceutical Market Research Association (page 21).
Fixed dose	DDDs based on the average use for preparations within a group without considering and comparing the strengths of the different preparations (page 26).
IMS	Intercontinental Medical Statistics. IMS produces marketing research statistics for the pharmaceutical industry (page 22).
INN	International nonproprietary names. The preferred substance name in the ATC-system (page 15).
Intermittent dosing	In therapeutic groups e.g. hormones, where many of the preparations are administered intermittently, the dose administered is divided by the number of days in the treatment period to obtain the average daily dose (page 26).
Maintenance dose	The dose preferred when establishing the DDD. Some drugs are used in different initial doses but this is not reflected in the DDD (page 23).
NLN	The Nordic Council on Medicines (page 10).
“Other” group	3rd or 4th level, often named X, used for substances not clearly belonging to any existing ATC 3rd or 4th level (page 18).
PBIRG	Pharmaceutical Business Intelligence and Research Group (page 21).
PDD	The Prescribed Daily Dose for a substance is determined from prescription studies, medical- or pharmacy records and patient interviews. The PDD must be related to the diagnosis on which the dosage is based (page 31).

Plain preparation	Preparations containing one active component (page 18).
Pseudo-double medication	The simultaneous use of two chemically different substances with similar pharmacodynamic properties (page 36).
U	Unit, both international as well as others (page 27).
UD	The unit dose is used when a DDD for various reasons cannot be given in amount of active ingredient (page 27).
USAN	United States Adopted Name (page 15).
WHO Collaborating Centre for Drug Statistics Methodology	The centre responsible for the development and maintenance of the ATC/DDD system (page 11).
WHO Collaborating Centre for International Drug Monitoring	A collaborating centre situated in Uppsala, Sweden, which receives spontaneous reports of suspected adverse reactions from national centres and carries the operational responsibilities for WHO's programme on International Monitoring (page 36).
WHO Drug Information	Published by WHO 4 times a year to bring issues of primary concern to drug regulators and pharmaceutical manufacturers to the attention of a wide audience of health professionals and policy-makers concerned with the rational use of drugs. Publishes the new ATC codes/DDD approved at the working group meetings (page 39, 41, 43). Can be ordered from: Marketing and Dissemination, World Health Organization, 1211 Geneva 27, Switzerland, Telephone: +41 22 791 24 76, Fax: +41 22 791 48 57 Email: publications@who.int
WHO International Working Group for Drug Statistics Methodology	WHO appointed experts in medicine and statistics who advise the collaborating centre in the assignment of ATC/DDD and carries out research into the use of these methodologies in drug utilization. The Working Group meets two times a year, normally March and October (page 12).
WHO Pharmacological Action and Therapeutic Use of Drugs – List of Terms	A standard list of terms in current use describing pharmacological action and therapeutic use of pharmaceuticals. All rights are reserved by WHO. Limited distribution (page 15).

ANNEX I



WHO COLLABORATING CENTRE FOR
DRUG STATISTICS METHODOLOGY

Postal address: P.O.Box 4404 Nydalen, 0403 Oslo, Norway
Visiting address: Marcus Thranes gate 6, 0473 Oslo, Norway
Telephone: +47 21078160, Telefax: +47 21078146, E-mail: whocc@fhi.no

Application form

ATC

DDD (Marketing authorization is needed)

Requested by: Name: Company: Address: Country: Email:	
Active ingredients (preferably INN names):	INN request number:
Brand name:	
Dosage form:	Strengths:
Manufacturer:	
Main indication*:	
Other indications*:	
Approved dose recommendations*:	
ATC code proposal:	DDD proposal:

* References should be given and submitted (e.g. from SPC)

Status concerning Marketing Authorization

Marketing Authorization (MA) has been approved in the following countries ¹⁾ :	Date of approval
MA application has been submitted in the following countries ¹⁾²⁾ :	Date of submission::

A MA application has not yet been submitted, but is planned (date): _____, in the following countries: _____

Documentation should be enclosed (in English only). Electronic versions of all enclosures should be forwarded to the Centre. Please note that no paper copies are required when the application is submitted electronically followed by our automatic receipt. Application for ATC/DDD is free of charge.

Enclosures:

Summary of Product Characteristics Additional product documentation Data on prescribed daily dose Additional dose documentation

Date/Signature:	Position:
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- 1) If the indication(s) in any country differ from those given in the application form, please describe these differences in a separate enclosure.
- 2) Please indicate type of application (e.g. National, Centralised Procedure, etc).

ANNEX II

ORDER FORM

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2011

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<i>ATC classification index without DDDs - ASCII format</i>	€ 160		English version only
<i>Guidelines for ATC classification and DDD assignment – PDF-format</i>	€ 50		

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