



World Health
Organization

Guidance on the Use of International Nonproprietary Names (INNs) for Pharmaceutical Substances

INNOVATION

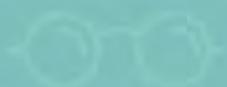


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GUIDANCE ON THE USE OF
INTERNATIONAL NONPROPRIETARY
NAMES (INN_s) FOR PHARMACEUTICAL
SUBSTANCES



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GUIDANCE ON THE USE OF INTERNATIONAL
NONPROPRIETARY NAMES (INNs)
for Pharmaceutical Substances

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1. General introduction

The present document on the use of INNs is intended as a general explanation of the INN selection process. They have been developed for drug regulatory authorities for use in the marketing authorization/registration of products, drug manufacturers who are requesting new INNs and those using INNs, patent authorities/offices, trademark attorneys and trademark specialists, scientists, teachers, health professionals, as well as any person interested in nomenclature.

1.1. General information on the INN system

An International Nonproprietary Name (INN) identifies a pharmaceutical substance or active pharmaceutical ingredient by a unique name that is globally recognized and is public property. A nonproprietary name is also known as a generic name.



The INN system as it exists today was initiated in 1950 by a World Health Assembly resolution WHA3.11 and began operating in 1953, when the first list of International Nonproprietary Names for pharmaceutical substances was published. The cumulative list of INNs now stands at some 9300 names designated since that time, and this number is growing every year by some 160 new INNs.

Since its inception, the aim of the INN system has been to provide health professionals with a unique and universally available designated name to identify each pharmaceutical substance. The existence of an international nomenclature for pharmaceutical substances, in the form of INNs, is important for the clear identification, sale prescription and dispensing of medicines to patients, and for communication and exchange of information among health professionals and scientists worldwide.

As unique names, INNs have to be distinctive in sound and spelling, and should not be liable to confusion with other names in common use. To make INNs universally available they are formally placed by WHO in the public domain, hence their designation as "nonproprietary". They can be used without any restriction whatsoever to identify pharmaceutical substances.

Another important feature of the INN system is that the names of pharmacologically-related substances demonstrate their relationship by using a common "stem". By the use of common stems the medical practitioner, the pharmacist, or anyone dealing with pharmaceutical products can recognize that the substance belongs to a group of substances having similar pharmacological activity. For example all iodine-containing contrast media are given the prefix *io-*, while all β -adrenoreceptor antagonists the suffix

-*olol*. The use of stems is described later in more detail.

The extent of INN utilization is expanding with the increase in the number of names. Its wide application and global recognition are also due to close collaboration in the process of INN selection with numerous national drug nomenclature bodies. The increasing coverage of the drug-name area by INNs has led to the situation whereby the majority of pharmaceutical substances used today in medical practice are designated by an INN. The use of INNs is already common in research and clinical documentation, while the importance of the programme is growing further due to expanding use of generic names for pharmaceutical products.

The names which are given the status of an INN are selected by the World Health Organization on the advice of experts from the WHO Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations. The process of INN selection follows three main steps:

- a request/application is made by the manufacturer or inventor,
- after a review of the request a proposed INN (prop. INN) is selected and published for comments,
- after a time-period for objections has lapsed, the name will obtain the status of a recommended INN (rec. INN) and is published as such.

The procedures relating to each of these steps are described in the present document in full detail.

INNs are selected in principle only for single, well-defined substances that can be unequivocally characterized by a chemical name (or formula). It is the policy of the INN Programme not to select names for mixtures of substances, while substances that are not fully characterized are included in the INN system in exceptional cases only. INNs are not selected for herbal substances (vegetable drugs) or for homoeopathic products. It is also the policy of the INN Programme not to select names for those substances that have a long history of use for medical purposes under well-established names such as those of alkaloids (e.g. morphine, codeine), or trivial chemical names (e.g. acetic acid).

The INN is usually designated for the active part of the molecule only, to avoid the multiplication of entries in cases where several salts, esters, etc. are actually used. In such cases, the user of the INN has to create a modified INN (INN_M) himself; *mepyramine maleate* (a salt of *mepyramine* with *maleic acid*) is an example of an INN_M. When the creation of an INN_M would require the use of a long or inconvenient name for the radical part of the INN_M, the INN Programme will select a short name for such a radical (for example, *mesilate* for *methanesulfonate*).

Names of pharmaceutical preparations, such as used in pharmacopoeia monograph titles, usually consist of two elements, the first designating the active substance (an INN is used here), and the other designating the dosage form of the product. Rules for creating such names fall outside the INN Programme and are not discussed here.

In the process of INN selection, the rights of existing trademark owners are fully protected. If in the period of four months following the publication of a proposed INN, a formal objection is filed by an interested person who considers that the proposed INN is in conflict with an existing trademark, WHO will actively pursue an arrangement to obtain a withdrawal of such an objection or will reconsider the proposed name. As long as the objection exists, WHO will not publish it as a recommended INN.

With the growing number of INNs and trademarks, the possibility of conflicts between the two has gradually increased, even with full protection of the rights of existing trademarks. The main source of conflict is usually an attempt by a manufacturer to propose a new trademark containing stems established in the INN Programme. If protection is granted to such a name, this may diminish the freedom of the INN Programme in selecting further INNs in the same series of substances. To prevent such occurrences, the matter was taken up in a resolution of the World Health Assembly WHA46.19. This issue is discussed in

more detail in section 4.

Further background information on the INN Programme may be found in Annex 1.

1.2. Use of INNs

Nonproprietary names are intended for use in pharmacopoeias, labeling, product information, advertising and other promotional material, drug regulation and scientific literature, and as a basis for product names, e.g. for generics. Their use is normally required by national or, as in the case of the European Community, by international legislation. As a result of ongoing collaboration, national names such as British Approved Names (BAN), Dénominations Communes Françaises (DCF), Japanese Adopted Names (JAN) and United States Accepted Names (USAN) are nowadays, with rare exceptions, identical to the INNs.

Some countries have defined the minimum size of characters in which the generic nonproprietary name must be printed under the trademark labeling and advertising. In several countries the generic name must appear prominently in type at least half the size of that used for the proprietary or brand name. In some countries it has to appear larger than the trademark name. Certain countries have even gone so far as to abolish trademarks within the public sector.

To avoid confusion, which could jeopardize the safety of patients, trademarks cannot be derived from INNs and, in particular, must not include their common stems. As already mentioned the selection of further names within a series will be seriously hindered by the use of a common stem in a brand name.

1.3. School of INN (SoINN)

The School of INN is a virtual body established under the auspices of the International Nonproprietary Names (INN) for Pharmaceutical Substances Programme of WHO with a vision to have the INN used by all stakeholders across the world as a common nomenclature for all pharmaceutical substances. This vision is to be achieved through empowerment of all stakeholders involved in research and development of pharmaceutical substances, manufacturing and regulatory control of pharmaceutical products, education and training of healthcare professionals, as well as the patients and consumers of healthcare services to use this common nomenclature that is understood throughout the value chain of research, education, practice, manufacture and regulation.

The role and function of the SoINN is to advocate for the correct and effective use of the INN throughout the Pharmaceutical value chain, to develop and raise interest in the Science of Pharmaceutical Nomenclature and to cultivate the future success and harmonisation of nomenclature programmes around the world. This will be done through regular publications and presentations to reach the pharmaceutical industry and health professionals; Education and training of students, industry and health professionals in the construct of INN to promote safe and effective use of medicine and to facilitate learning; Outreach to pharmaceutical industry and patients or consumers to facilitate understanding of INN and how correct use would enhance pharmaceutical outcomes.

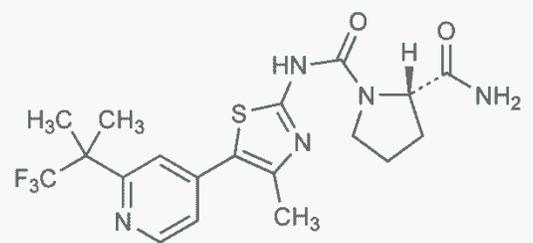
The SoINN shall, within the INN Programme, endeavour to propose names that are more user friendly without compromising the essence of the science and information contained within a pharmaceutical product name.

2. Elements in the INN system

2.1. Proposed INNs

The selection of a new INN relies on a strict procedure. Upon receipt of an INN request form, the WHO Secretariat examines the suggested names for conformity with the general rules, for similarities with published INNs and potential conflicts with existing names, including published INNs and trademarks. A note summarizing the result of these checks is added and the request is subsequently forwarded to the INN experts for comments. Once all experts agree upon one name, the applicant is informed of the selected name.

Newly selected, proposed INNs are then published in *WHO Drug Information*, which indicates a deadline for a 4-month objection period. This period is allowed for comments and/or objections to the published names to be raised. The reasons for any objection must be stated clearly and these will be evaluated by the experts for further action. Users are invited to refrain from using the proposed name until it becomes a recommended INN, in order to avoid confusion should the name be modified. Two lists of proposed INNs are published yearly. An example is set out below.

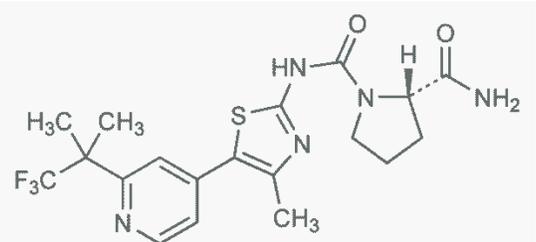
alpelisibum		
alpelisib	(2 <i>S</i>)- <i>N</i> ¹ -{4-methyl-5-[1-(1,1,1-trifluoro-2-methylpropan-2-yl)pyridin-4-yl]-1,3-thiazol-2-yl}pyrrolidine-1,2-dicarboxamide <i>antineoplastica</i>	
alpélisib	(2 <i>S</i>)- <i>N</i> ¹ -{4-méthyl-5-[1-(1,1,1-trifluoro-2-méthylpropan-2-yl)pyridin-4-yl]-1,3-thiazol-2-yl}pyrrolidine-1,2-dicarboxamide <i>antineoplasique</i>	
alpelisib	(2 <i>S</i>)- <i>N</i> ¹ -{4-metil-5-[1-(1,1,1-trifluoro-2-metilpropan-2-il)piridin-4-il]-1,3-tiazol-2-il}pirrolidina-1,2-dicarboxamida <i>antineoplásico</i>	
	C ₁₉ H ₂₂ F ₃ N ₅ O ₂ S	1217486-61-7
		

2.2. Recommended INNs

The final stage of the selection process is the recommended INN. Once a name has been published as a recommended INN it will not normally be modified further and is ready for use in labeling, publications, on drug information. It will serve to identify the active pharmaceutical substance during its lifetime worldwide. Since the name is available in the public domain it may be used freely. However, it should not be registered as a trademark since this would prevent its use by other parties (see also chapter 4).

Recommended INNs are published in the *WHO Drug Information* as a consequence of the objection procedure applied to proposed INNs (see 2.1 above). As from 1997, two lists of proposed INNs are published yearly and as from list 37 of recommended INNs, graphic formulae are also included for better identification of the substances.

An example of an entry in the list may be found below:

alpelisib	(2S)-N ¹ -{4-methyl-5-[1-(1,1,1-trifluoro-2-methylpropan-2-yl)pyridin-4-yl]-1,3-thiazol-2-yl}pyrrolidine-1,2-dicarboxamide
alpelisib	(2S)-N ¹ -{4-méthyl-5-[1-(1,1,1-trifluoro-2-méthylpropan-2-yl)pyridin-4-yl]-1,3-thiazol-2-yl}pyrrolidine-1,2-dicarboxamide
alpelisib	(2S)-N ¹ -{4-metil-5-[1-(1,1,1-trifluoro-2-metilpropan-2-il)piridin-4-il]-1,3-tiazol-2-il}pirrolidina-1,2-dicarboxamida
	C ₁₉ H ₂₂ F ₃ N ₅ O ₂ S
	

2.3. Names for radicals and groups

During the 1975 meeting on Nonproprietary Names for Pharmaceutical Substances the experts discussed the issue of INNs for salts and esters and noted that requests had frequently been received for INNs for salts, esters, or combination products of substances for which INNs already existed. At that time, the experts decided that INNs for the simple salt and esters should be devised from the INN in conformity with normal chemical practice.

Some of the radicals and groups involved are, however, of such complex composition that it makes it inconvenient to use the chemical nomenclature. It was thus decided that in such cases, shorter nonproprietary names are selected for these inactive moieties and published in proposed lists under the title "Names for Radicals and Groups". Separate names for salts and esters derived from this procedure are not published. If a "radical and group name" is used in conjunction with an INN, they are referred to as International Nonproprietary Name (Modified) or INN^M.

A comprehensive list of radicals and groups may be obtained from the Distribution and Sales unit or the INN Secretariat (INN.s: *Names for radicals and groups combined summary list, WHO/EMP/RHT/TSN/2015.1, updated regularly*).
<http://www.who.int/entity/medicines/services/inn/RadicalBook2015.pdf?ua=1>

2.4. Modified INNs (INN^Ms)

In principle, INNs are selected only for the active part of the molecule, which is usually the base, acid or alcohol. In some cases, however, the active molecules need to be expanded for various reasons, such as formulation purposes, bioavailability or absorption rate. In 1975 the experts designated for the selection of INN decided to adopt a new policy for naming such molecules. In future, names for different salts or esters of the same active substance should differ only with regard to the inactive moiety of the molecule. For example, *oxacillin* and *ibufenac* are INNs and their salts are named *oxacillin sodium* and *ibufenac sodium*. The latter are called modified INNs (INN^Ms).

Before the existence of this rule, some INNs were published for salts. In such cases, the term "modified INN" may also be used for a base or acid. For example, *levothyroxine sodium* was published as an INN

and *levothyroxine* may thus be referred to as an INN_M.

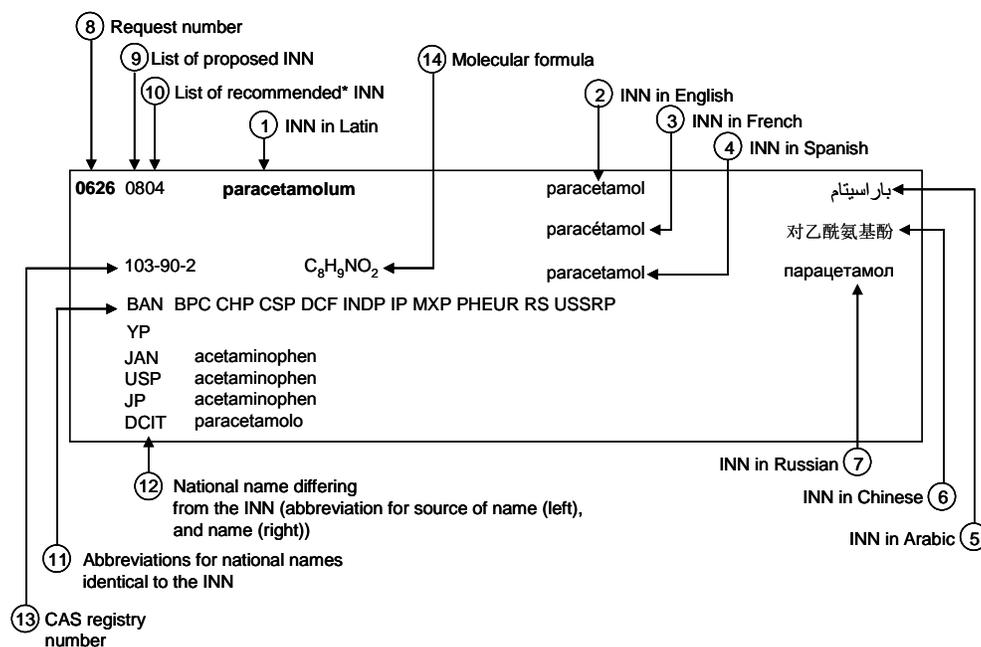
Please see also chapter 2.3 for radicals and groups which are used in conjunction with INNs and which are also referred to as INN_M, and the document *International Nonproprietary Names Modified, INN Working Document 05.167/3*.

2.5. Cumulative list

All names selected as proposed and recommended INNs are published in a *Cumulative list*, which is updated periodically. The generic names are presented in alphabetical order by Latin name. Each entry includes:

- equivalent nonproprietary names: : in Latin, English, French, Spanish, Arabic, Chinese and Russian, as well as reference to other common names;
- a reference to the INN list in which the name was originally proposed or recommended, or last amended;
- reference to names of substances that have been abandoned or never been marketed;
- reference to national nonproprietary names;
- reference to pharmacopeial monographs or similar official references;
- reference to names issued by the International Organization for Standardization (ISO);
- reference to the Convention of Psychotropic Substances, if applicable;
- reference to the List of Narcotic Drugs under International Control, if applicable;
- the molecular formula;
- its Chemical Abstracts Service (CAS) number.

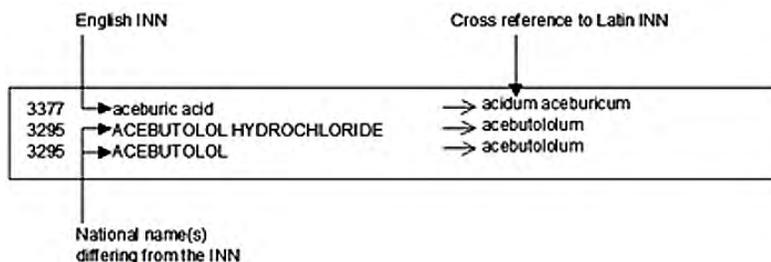
The layout for information contained in the *Cumulative list* of INNs is as follows:



* An asterisk in place of a recommended list number signifies that an objection has been raised to the proposed name.

Note: Cross-references are provided for entries corresponding to (a) English, French and Spanish INN that appear in different alphabetical positions from the Latin INN and (b) national names that differ from the INN. Entries for (a) are printed in lower-case letters (as in the example of aceburic acid, below) while

entries for (b) are printed in capitals (as in the examples of ACEBUTOLOL HYDROCHLORIDE and ACEBUTO- LOLO)



3. Principles for selection of INNs

3.1. General rules

General rules were established at the beginning of the INN Programme in order to guide the members of the INN Expert Group and to allow health professionals to understand the rationale for a number of new names. At first, some countries used shortened chemical names as generic names, but this system was found to be very limited, since many molecules contain similar elements and groups, such as phenol, chlorine, methyl or benzene-rings, in their chemical structures. In addition, a name that indicates relationship to a group of pharmacological similarly-acting substances is more meaningful to users.

In its Twentieth Report (WHO Technical Report Series, No. 581, 1975), the WHO Expert Group on Nonproprietary Names for Pharmaceutical Substances reviewed the general principles for devising, and the procedures for selecting, international nonproprietary names (INN) in the light of developments in pharmaceutical compounds over the years. The current version of the *General principles for guidance in devising international nonproprietary names for pharmaceutical substances* is reproduced in Annex 2.

3.2. Use of stems

Usually, an INN consists of a random, fantasy prefix and a common stem; substances belonging to a group of pharmacologically related substances show their relationship by the use of a common stem. Sometimes sub-stems are established to differentiate between different related groups of substances, e.g. *-olol* for β -adrenoreceptor antagonists and antihypertensive, *-teplase* for tissue-type-plasminogen activators and *-uplase* for urokinase-type-plasminogen activators.

A list of common stems used in the selection of INNs may be found in Annex 3.

3.3. Stereoisomers

An INN for a new chemical entity does not routinely specify the stereoisomeric state of the molecule in the nonproprietary name. If the stereochemistry has been determined, then this information is presented in the chemical name(s) to identify the substance. An INN can, therefore, identify the racemic mixture (e.g. ibuprofen, tetramisole), the *levo*- isomer (e.g. amifostine, lofentanil, prenalterol, remoxipride, quadazocine), or the *dextro* form (e.g. butopamine). Subsequently if an INN is needed for a different enantiomer or for the racemic form, the following prefixes should be added to the existing INN:

- For the *levo* form, the *lev-/levo-* prefix is used, e.g. levocarnitine, levamisole.
- For the *dextro* form, the *dex-* prefix is used, e.g. dexamisole, dexibuprofen.
- For the *racemic* form, the *rac-/race-* prefix is used, e.g. racepinefrine.

3.4. Radioactive compounds

A name for a drug substance containing a radioactive atom should list, in the following order:

- 1) the name of the substance containing the radioactive atom,
- 2) the isotope number,
- 3) the element symbol, and
- 4) the name of the carrier agent, if any,

e.g. cyanocobalamin (^{60}Co), technetium ($^{99\text{m}}\text{Tc}$) bicipitate, technetium ($^{99\text{m}}\text{Tc}$) sestamibi.

3.5. Specific groups of biological substances

INNs have been assigned to biological substances since the early days of the INN Programme. As well as many names for individual substances, animal insulin preparations were given an INN in Recommended list 3 in 1959. In the period up to 1980, names were assigned to antibiotics, synthetic peptides, hormones and other proteins.

In 1982, the name *insulin human* was proposed for the recombinant protein identical to natural human insulin, and since then names have been assigned to a growing number of recombinant substances. Within the INN Programme, names have not been assigned to natural human blood products or vaccines. For those groups of biological products, the WHO Expert Committee on Biological Standardization (ECBS) has been adopting the scientific names of the biological products within the definitions of respective requirements.

Since the time when *insulin human* became the first recommended INN (rINN) for a recombinant substance, the range of biological/biotechnological substances has increased in size and complexity. For example, new stems have been introduced for tissue plasminogen activators (*-plase*) among other groups. Recombinant glycosylated proteins with the same protein sequence but produced in different cell systems have been classified using Greek letters as indicators in the sequence of submission for an INN, for example erythropoietin gives *epoetin alfa*, *epoetin beta* and so on. In the 1990s, a systematic scheme for naming monoclonal antibodies was implemented, based on the stem *-mab*, which indicates the origin (human, mouse etc.) of the antibody and its intended use: for example tumour, immunomodulator and so on.

As a result of the scientific and technical developments over the past few years and continuing now, new substances of biotechnology and other biological substances have been developed and approved for clinical use and more substances can be expected for the treatment or prevention of disease. Examples include recombinant human proteins expressed in animals or plants and gene and cell therapies.

Annex 4 summarizes the nomenclature of biological and biotechnological substances (for details and examples please see the document WHO/EMP/RHT/TSN/2016.1: *International Nonproprietary Names (INN) for biological and biotechnological substances (a review)*, updated regularly).

4. Protection of INNs

Lists of both proposed and recommended INNs are sent together with a *note verbale* by the Director-General to WHO Member States (at present 194), to national pharmacopoeia commissions and to other bodies designated by Member States. In her *note verbale*, the Director-General of the World Health Organization requests that Member States should take such steps as are necessary to prevent the acquisition of proprietary rights on the name, including prohibiting registration of the name as a trade name.

Over the years, the need to maintain the integrity of the INN system has become urgent. This is reflected

in the following extract from the Fifth Report of the WHO Expert Committee on the Use of Essential Drugs, which met in November 1991¹:

"The procedure for selecting INNs allows manufacturers to contest names that are either identical or similar to their licensed trademarks. In contrast, trademark applications are disallowed, in accordance with the present procedure, only when they are identical to an INN. A case for increased protection of INNs is now apparent as a result of competitive promotion of products no longer protected by patents. Rather than marketing these products under generic name, many companies apply for a trademark derived from an INN and, in particular, including the INN common stem. This practice endangers the principle that INNs are public property; it can frustrate the rational selection of further INNs for related substances, and it will ultimately compromise the safety of patients by promoting confusion in drug nomenclature."

These concerns were debated during the sixth International Conference of Drug Regulatory Authorities (ICDRA), in Ottawa, in October 1991. Based on recommendations made by the WHO Expert Committee on the use of Essential Drugs the resolution WHA46.19 on Nonproprietary Names for pharmaceutical substances was adopted in May, 1993 during the Forty-sixth World Health Assembly requesting Member States to:

- *"enact rules or regulations, as necessary, to ensure that international nonproprietary names (or the equivalent nationally approved generic name used in the labeling and advertising of pharmaceutical products are always displayed prominently;*
- *to encourage manufacturers to rely on their corporate name and the international nonproprietary names, rather than on trademarks, to promote and market multisource products introduced after patent expiration;*
- *to develop policy guidelines on the use and protection of international nonproprietary names, and to discourage the use of names derived from INNs, and particularly names including established INN stems as trade-marks."*

In the Director-General's *note verbale* attention is drawn to this resolution concerning the use and protection of International Nonproprietary Names (INNs). The full text of the resolution is reproduced in Annex 5.

As a matter of principle, it may thus be recommended that trademarks should not be derived from INNs. In particular, the intentional incorporation of meaningful INN stems in trademarks should be avoided.

Similarly, inclusion of elements from biochemical nomenclature (like *-feron* from interferon, or *-leukin* from interleukin) in trademarks in anticipation is discouraged since these elements are likely to be utilized as stems within the INN nomenclature. Their inclusion in trademarks could pre-empt the logical development of the INN nomenclature. In accordance with resolution WHA46.19, registration of an INN together with a firm's name is perfectly acceptable, as long as it does not prevent another manufacturer from using the same approach. More information can be found in the trademark leaflet, *Information Leflet for Trademark Departments*.

¹ WHO Technical Report Series, No. 8:25, 1992.

5. How to apply for an INN

5.1. Procedure for selection of INNs

The selection of INNs is based on the *Procedure for selection of international nonproprietary names for pharmaceutical substances*. The text adopted is set out in World Health Assembly resolution WHA3 .11 [Text adopted by the Executive Board of WHO in resolution EB15.R7 (Off. Rec. World Health Organization, 1955,60, 3) and amended by the Board in resolution EB43.R9 (Off. Rec. World Health Organization, 1969,173, 10).]. In order to request an INN, the use of the online application form is mandatory (https://extranet.who.int/tools/inn_online_application/). A fact simile of the application/request form for INN is attached as Annex 7 in its updated version.

In countries with national nomenclature commissions, applications for international nonproprietary names should be made through the national authorities. In countries without a national nomenclature commission, requests for INNs should be applied for using the INN online service. According to the described process, the hard copy of the application for INNs should be addressed to:

**World Health Organization
International Nonproprietary Names
(HSS/EMP/INN)
20, Avenue Appia
1211 Geneva 27
Switzerland
E-Mail: innprogramme@who.int
Fax : +41 22 791 4856/5853
Tel. : +41 22 791 1249**

5.2. INN request form

Before a suggested name can be evaluated by the INN Secretariat, complete information must be provided on a request form to facilitate uniform handling of the data and to assure that pertinent items have not been omitted. It is important that the information is as comprehensive as possible. If parts of this information are missing or explanations are unclear or incomplete, the INN Secretariat will request the applicant to furnish the missing data. This can result in delay because selection of an INN requires the availability of all relevant information to the INN experts.

The following explanations will help applicants to complete the INN form. If additional information is needed, an applicant may contact the INN Secretariat at the World Health Organization, EMP/RHT/TSN/INN, 20 Avenue Appia, CH-1211 Geneva 27, Switzerland. (Telephone: +41 22 791 1249. Facsimile: +41 22 791 4856/5853. Internet: innprogramme@who.int).

Suggested names in order of preference

An applicant may make 6 suggestions for an INN relating to the acid, base or alcohol of a specific chemical entity under investigation. The suggested name should be a single word and not inconveniently long.

Nonproprietary names are developed by a system that relates compounds with chemical, pharmacological or therapeutic similarity. Therefore, whenever justified, the suggested name must incorporate the established common stem. A list of stems may be found in the document entitled *The use of common stems in the selection of international nonproprietary names (INN) for pharmaceutical substances (WHO/PHARM S/NOM 15)* which is updated regularly.

Occasionally stems require modification. For example, some drugs inhibit α -adreno-receptors as well as

β -adrenoreceptors and exhibit a specific structural variation from the "-olol" prototype. Accordingly, for this type of drug, the stem was modified by one letter to "-alol". This change introduces a nuance in the naming of related groups of drugs that may not be apparent to every observer but would be understood by someone familiar with the naming conventions of the β -adrenoreceptor antagonists and related compounds. The important point is that similar compounds have a common element in the name that imparts useful information.

It is imperative that the newly suggested name does not conflict with existing chemical names, other nonproprietary names or trademarks. Therefore, the INN Secretariat requests the applicant to verify the absence of conflicts with existing chemical names, common names for insecticides, other nonproprietary names, and trademarks. Some firms routinely perform exhaustive searches for possible conflicts with a suggested INN and for pharmacologically and chemically related compounds with already assigned INNs; the INN Secretariat would appreciate receiving this information to avoid search duplication.

Chemical name and description

Chemical information should be as complete and as current as possible. Information on stereochemistry should be included if known. The chemical names will be in accordance with the nomenclature rules of the International Union of Pure and Applied Chemistry (IUPAC); the Chemical Abstracts Index names in their current style may also be included as additional information. The chemical name provided by the manufacturer is reviewed for accuracy and to confirm that its construction follows accepted chemical nomenclature rules.

A description is used to identify a substance that is insufficiently defined to be assigned an IUPAC and CAS chemical name. This description will be superseded by the chemical name when the drug substance is fully characterized.

Precautions are taken to ensure confidentiality of the material submitted to WHO, but an applicant should not attempt to obtain an INN before all patent procedures are completed and until full chemical information can be made available to WHO.

Graphic formula

Without a graphic formula, it may be difficult to determine if an INN already exists. In addition, the graphic formula is necessary to relate the new drug to existing compounds in the same chemical family. Guidelines for drawing structures may be found in the document entitled *Graphic representation of chemical formulae in the publications of International Nonproprietary Names for pharmaceutical substances (WHO/PHARM/95.579)*, available from the INN Secretariat upon request. In case of biological substances the graphic formula must be provided in text format (MS word document or text).

Molecular formula

A one-line molecular formula constructed in accordance with accepted chemical practices should be supplied. The molecular formulas should be given in the following manner, e.g. $C_{21}H_{28}N_2$. In case of biological substances the molecular formula can be omitted.

Chemical Abstracts Service (CAS) registry number

The CAS registry number should be submitted to the INN Secretariat and included on the INN request form. If no number has yet been assigned, the manufacturer should obtain the CAS registry number, if applicable, from Chemical Abstracts Services for data validation and publication in the INN Proposed lists. Proof of the entry will be required. In case of substances for cell based therapies, the CAS registry number can be omitted.

Tradenames (known or contemplated)

If a trademark has been issued for the drug, it should be entered on the form. List any national or international trademarks (and manufacturers) and the name of the country where the trademark is registered.

Any other name or code

Sometimes, long before a nonproprietary name or a trademark has been selected for a new compound, it may acquire a trivial name that has been used in the laboratory and scientific literature. The INN Secretariat would like to be made aware of such names but requests manufacturers not to create, use, or in any way encourage the creation of trivial names for new drugs. The fact that a trivial name has become accepted in the literature will not ensure its adoption as a nonproprietary name and may only cause confusion when an official nonproprietary name is selected. It is therefore recommended to use codes before the publication of a recommended nonproprietary name and indicate these on the request form to the INN Secretariat as an additional reference.



Principal therapeutic use(s) and posology

It is important to know the therapeutic; category for the new compound as such information may determine the stem selected for the nonproprietary name. Pertinent reprints presenting evidence of the claimed therapeutic use should be included with the application (for terminology, please see *Pharmacological Action and Therapeutic Use of Drugs*, a list of terms, English/French/Spanish, 1997 (WHO/PHARM/97.594).

Pharmacological action

The pharmacological action should be explained in as much detail as possible, since it may also influence the stem selected for the compound. Again, pertinent reprints must be included to support the claimed action (for terminology, please see above).

Date of clinical trial

As a general guide, the development of a drug should progress up to the point of clinical trials (phase II) before an application is submitted to the INN Secretariat for name selection. An approximate date when clinical trials began is requested. The intent of this request is to assure that clinical trials are under way. It is the belief that if a drug has entered clinical trials, there is a reasonable expectation that it will be

marketed and thus the name selected will have been developed for that need and purpose.

In case the development is stopped, the manufacturer should inform the INN Secretariat as soon as possible, in order to halt the selection process.

Availability of suggested names

The originator of the INN request confirms with his signature that the suggestion is made on the understanding that, insofar as is known, none of the suggested names are either registered or pending registration.

Permission to publish the CAS registry number

The applicant herewith confirms that the CAS registry number sent to the INN Secretariat is correct and may be used in the INN lists.

Additional comments

This section allows the applicant to give additional comments and/or information.

6. References for supporting material

All INN and related information are also now available in digital format on the internet and on searchable databases.

The INN users can access INN MedNet and by using a common browser, search by name in English, French, Chinese, Spanish, Arabic, Russian and Latin and by list (Proposed and Recommended). The MedNet INN users community is the largest WHO community reaching more than 14.000 INN stakeholders all over the world (see below).

Moreover, INN Programme provides the INN Global Data Hub for institutions requiring it. This is a web service enabling an interoperable machine-to-machine interaction over the network. It has an interface described in a machine-processable format. Other systems interact with the Web service in a manner prescribed by its description using the INN Hub API messages conveyed using HTTP protocol.

The INN Global Data Hub allows transparent integration of the INN database on web site and/or applications.

For an off line use, the CD Rom of the Cumulative List is published every two years.

6.1. Documents:

- *The use of common stems in the selection of international nonproprietary names (INN) for pharmaceutical substances* (originally WHO/PHARM S/NOM 15; WHO/EMP/RHT/TSN/2013.1) INN Programme, WHO, Geneva – addendum and List of pre-stems are regularly updated on the INN Web site
- *Graphic representation of chemical formulae in the publications of international nonproprietary names (INN) for pharmaceutical substances* (WHO/PHARM/95.579), INN Programme, WHO, Geneva
- *Pharmacological Action and Therapeutic Use of Drugs, list of terms*, English/French Spanish, 1997, (WHO/PHARM/97.594), WHO, Geneva

- *INN for Pharmaceutical Substances: Names for radicals and groups and others, comprehensive list*, WHO/EMP/RHT/TSN/2015.1, INN Programme, WHO, Geneva - updated regularly
- *International Nonproprietary Names (INN) for biological and biotechnological substances (a review)*, 2016, WHO/EMP/RHT/TSN/2016.1, INN Programme, WHO, Geneva
- *Definition of INNs for Substances Prepared by Biotechnology*, PHARM S/NOM 1348, INN Programme, WHO, Geneva
- *International Nonproprietary Names Modified*, INN Working Document 05.167/3

6.2.Publications:

- *Cumulative List of INNs, No. 15*, 2014, WHO, Geneva
- *WHO Drug Information* (quarterly journal published by the World Health Organization)
- *Information leaflet for Trademark Departments*, INN Programme, WHO, Geneva

6.3.Websites

- INN Programme:
<http://www.who.int/medicines/services/inn/en/>
- Online application:
https://extranet.who.int/tools/inn_online_application/
- Radical Book:
<http://www.who.int/entity/medicines/services/inn/RadicalBook2015.pdf?ua=1>
- MedNet:
<https://mednet-communities.net/inn/>

Background information on the INN Programme

The activities of national nomenclature commissions are coordinated in order to achieve international standardization in nomenclature under the auspices of WHO according to article 2a and 2u of its constitution (adopted in 1946 in New York):

"In order to achieve its objective, the functions of the World Health Organization shall be:
 (a) to act as the directing and coordinating authority on international health work;...
 (u) to develop, establish and promote international standards with respect to food, biological, pharmaceutical and similar products; ... "

The WHO Programme on the selection of international nonproprietary names (INN) emerged really as an extension of the WHO Programme on the unification of pharmacopoeias and the preparation of the International Pharmacopoeia requested by the very first World Health Assembly in July 1948 in resolution WHA1.21. The meeting of an Expert Committee on Unification of Pharmacopoeias in 1949 studied the preparation of general rules for nomenclature, and drew up a plan that was adopted in 1950 by a resolution of the World Health Assembly (WHA3.11).

The World Health Organization's (WHO) international nomenclature programme was thus established in 1953 when Member countries adopted a resolution at the World Health Assembly officially initiating the programme on International Nonproprietary Names (INN) for pharmaceutical substances [French : Dénominations Communes Internationales]; [Spanish : Denominaciones Comunes Internacionales - DCI].

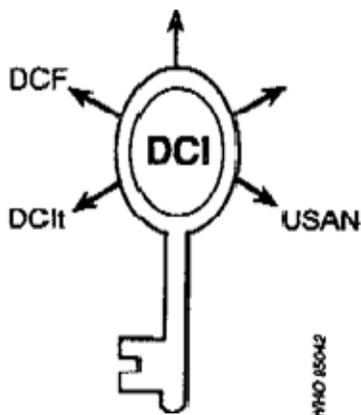
The official "Procedure for the Selection of Recommended International Nonproprietary Names for Pharmaceutical Substances" and the "General Principles for Guidance in Devising International Nonproprietary Names for Pharmaceutical Substances" on which the whole programme is based were adopted by the Executive Board in 1955 in resolution EB 15.R7. The Procedure has remained unchanged -- except for the replacement of the words "INNs for Pharmaceutical Preparations" by "*INNs for Pharmaceutical Substances*" (res. *EB43.R9*). However, the General Principles have evolved and revisions were regularly approved in the reports of the Sub-Committee meetings submitted to the Executive Board. Since 1969 the Director-General is authorized by the Executive Board to make such revisions of the General Principles as may seem desirable in the light of advances in science and of experience as may be suggested by the members of the Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations designated to deal with the selection of nonproprietary names (INN experts) in accordance with the above-mentioned Procedure (res. *EB31.R9*).

From 1950 onwards the programme was dealt with by the Sub-Committee of the Expert Committee on the Unification of Pharmacopoeias. The first task of the Sub-Committee was to establish contacts with national pharmacopoeia commissions that had already established programmes on the unification of drug nomenclature as those carried out under the *Comité de Nomenclature* of the *Commission permanente de la Pharmacopée Française*, the Nomenclature Committee of the British Pharmacopoeia Commission, the Council of Drugs of the American Medical Association in the USA and the Nomenclature Committee of the Nordic Pharmacopoeia Council in the Scandinavian countries. The purpose of these contacts was to coordinate the activities of such existing national nomenclature programmes.

Between 1950 and 1966 the Sub-Committee met 16 times. The earlier meetings were concerned with developing the Procedure and the General Principles and the first list of proposed INNs was only published in 1953. In 1967 the Sub-Committee became the Expert Group on Nonproprietary Names for Pharmaceutical Preparations and later the Expert Group on Nonproprietary Names for Pharmaceutical

Substances. This Expert Group only met in 1967, 1968, 1970 and 1975. In the other years, and since 1976, the meetings were held in a less formal way and referred to as Consultations on the Selection of INNs. The justification for this less formal approach is that the main report of the INN Expert Group consists of the officially published INNs selected during its meetings.

The composition of the INN meetings over almost 50 years has been characterized by a great stability. The average number of participants is 20 experts, mostly people with responsible positions in or secretaries of national nomenclature commissions and only some 40 people have been involved over the years. At present the INN Expert Group is composed of experts from Australia, Burkino Faso, China, France, Germany, Italy, Japan, Panama, Poland, Russia, Singapore, South Africa, Spain, Syria, Tunisia, the United Kingdom and USA.



- BAN: British Approved Name**
- DCF: Dénomination Commune Française**
- DCIT: Denominazione Comune Italiana**
- JAN: Japanese Accepted Name**
- USAN: United States Approved Name**

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General principles for guidance in devising International nonproprietary names for pharmaceutical substances

1. International Nonproprietary Names (INN) should be distinctive in sound and spelling. They should not be inconveniently long and should not be liable to confusion with names in common use.
2. The INN for a substance belonging to a group of pharmacologically related substances should, where appropriate, show this relationship. Names that are likely to convey to a patient an anatomical, physiological, pathological or therapeutic suggestion should be avoided.

These primary principles are to be implemented by using the following secondary principles:

3. In devising the INN of the first substance in a new pharmacological group, consideration should be given to the possibility of devising suitable INN for related substances, belonging to the new group.
4. In devising INN for acids, one-word names are preferred; their salts should be named without modifying the acid name, e.g. "oxacillin" and "oxacillin sodium", "ibufenac" and "ibufenac sodium".
5. INN for substances which are used as salts should in general apply to the active base or the active acid. Names for different salts or esters of the same active substance should differ only in respect of the name of the inactive acid or the inactive base.

For quaternary ammonium substances, the cation and anion should be named appropriately as separate components of a quaternary substance and not in the amine-salt style.

6. The use of an isolated letter or number should be avoided; hyphenated construction is also undesirable.
7. To facilitate the translation and pronunciation of INN, "f" should be used instead of "ph", "t" instead of "th", "e" instead of "ae" or "oe", and "i" instead of "y"; the use of the letters "h" and "k" should be avoided."

When devising an INN it is important to be aware of possible language problems. Since the name is used worldwide, not only should certain letters be avoided, but experts need to be aware of unsuitable connotations in the major languages spoken in the world.

8. Provided that the names suggested are in accordance with these principles, names proposed by the person discovering or first developing and marketing a pharmaceutical preparation, or names already officially in use in any country, should receive preferential consideration.
9. Group relationship in INN (see Guiding Principle 2) should if possible be shown by using a common stem. The following list contains examples of stems for groups of substances, particularly for new groups. There are many other stems in active use. Where a stem is shown without any hyphens it may be used anywhere in the name.

<i>Latin</i>	<i>English</i>	
-acum	-ac	anti-inflammatory agents of the ibufenac group
-actidum	-actide	synthetic polypeptides with a corticotropin-like action
-adolum	-adol }	analgesics

-adol-	-adol-}	analgesics
-astum	-ast	antiasthmatic, antiallergic substances not acting primarily as antihistaminics
-astinum	-astine	antihistaminics
-azepamum	-azepam	diazepam derivatives
-bactamum	-bactam	β -lactamase inhibitors
bol	bol	steroids, anabolic
-buzonum	-buzone	anti-inflammatory analgesics, phenylbutazone derivatives
-cain-	-cain-	antifibrillant substances with local anesthetic activity.
-camum	-caine	local anesthetics
cef-	cef-	antibiotics, cephalosporanic acid derivatives
-cillinum	cillin	antibiotics, derivatives of 6-amino- penicillanic acid
-conazolium	-conazole	systemic antifungal agents, miconazole derivatives
cort	cort	corticosteroids, except prednisolone deivatives
-dipinum	-dipine	calcium channel blockers, nifedipine derivatives
fibratum	-fibrate	clofibrate derivatives
gest	gest	steroids, progestogens
gli-	gli-	sulfonamide hypoglycaemics
io-	io-	iodine-containing contrast media
-ium	-ium	quaternary ammonium compounds
-metacinum	-metacin	anti-inflammatory substances, indomethacin derivatives
-mycinum	-mycin	antibiotics, produced by Streptomyces strains
-nidazolium	-nidazole	antiprotozoal substances, metronidazole derivatives

-ololum	-olol	β -adrenoreceptor antagonists
-oxacinum	-oxacin	antibacterial agents, nalidixic acid derivatives
-pridum	-pride	sulpiride derivatives
-pril(at)um	-pril(at)	angiotensin-converting enzyme inhibitors
-profenum	-profen	anti-inflammatory substances, ibuprofen derivatives
prost	prost	prostaglandins
-relinum	-relin	hypophyseal hormone release-stimulating peptides
-terolum	-teroi	bronchodilators, phenethylamine derivatives
-tidinum	-tidine	histamine H ₂ -receptor antagonists
-trexatum	-trexate	folic acid antagonists
-verinum	-verine	spasmolytics with a papaverine-like action
vin-	vin-)	vinca alkaloids
-vin-	-vin-)	vinca alkaloids

List of common stems used in the selection of INNs

The following information has been extracted from the document: *The use of common stems in the selection of international nonproprietary names (INN) for pharmaceutical substances* (originally WHO/PHARM S/NOM 15; WHO/EMP/RHT/TSN/2013.1) INN Programme, WHO, Geneva – addendum and List of pre-stems are regularly updated on the INN Web site

STEM	DEFINITION
	<i>substem, if available</i>
<i>-abine (see -arabine and -citabine)</i>	arabinofuranosyl derivatives; nucleosides antiviral or antineoplastic agents, cytarabine or azacitidine derivatives
<i>-ac</i>	anti-inflammatory agents, ibufenac derivatives
<i>-acetam (see -racetam)</i>	amide type nootrope agents, piracetam derivatives
<i>-actide</i>	synthetic polypeptide with a corticotropin-like action
<i>-adol/-adol-</i>	analgesics
<i>-adom</i>	analgesics, tifludom derivatives
<i>-afenone</i>	antiarrhythmics, propafenone derivatives
<i>-afil</i>	inhibitors of phosphodiesterase PDE5 with vasodilator action
<i>-aj-</i>	antiarrhythmics, ajmaline derivatives
<i>-al</i>	aldehydes
<i>-aldrate</i>	antacids, aluminium salts
<i>-alol (see -olol)</i>	aromatic ring related to <i>-olols</i>
<i>-alox (see -ox)</i>	antacids, aluminium derivatives
<i>-amivir (see vir)</i>	neuraminidase inhibitors
<i>-ampanel</i>	antagonists of the ionotropic non-NMDA (<i>N</i> -methyl-D-aspartate) glutamate receptors (Namely the AMPA (amino-hydroxymethyl-isoxazole-propionic acid) and/or KA (kainite antagonist) receptors)
<i>andr</i>	steroids, androgens

<i>-anib</i>	angiogenesis inhibitors
<i>-anide</i>	-
<i>-anserin</i>	serotonin receptor antagonists (mostly 5-HT ₂)
<i>-antel</i>	anthelmintics (undefined group)
<i>-antrone</i>	antineoplastics; anthraquinone derivatives
<i>-apine (see -pine)</i>	tricyclic compounds
<i>-apt-</i>	aptamers, classical and mirror ones
<i>-(ar)abine</i>	arabinofuranosyl derivatives
<i>-arit</i>	antiarthritic substances, acting like clobuzarit and lobenzarit, (mechanism different from anti-inflammatory type substances, e.g. -fenamates or -profens)
<i>-arol</i>	anticoagulants, dicoumarol derivatives
<i>-arone</i>	-
<i>-arotene</i>	arotinoid derivatives
<i>arte-</i>	antimalarial agents, artemisinin related compounds
<i>-ase</i>	enzymes
<i>-ast</i>	antiasthmatics or antiallergics, not acting primarily as antihistaminics
<i>-astine</i>	antihistaminics
<i>-asvir (see -vir)</i>	antivirals, Hepatitis C Virus (HCV) NS5A inhibitors
<i>-azam (see -azepam)</i>	diazepam derivatives
<i>-azenil</i>	benzodiazepine receptor antagonists/agonists (benzodiazepine derivatives)
<i>-azepam</i>	diazepam derivatives
<i>-azepide</i>	cholecystokinin receptor antagonists, benzodiazepine derivatives
<i>-azocine</i>	narcotic antagonists/agonists related to 6,7-benzomorphan
<i>-azolam (see -azepam)</i>	diazepam derivatives
<i>-azoline</i>	antihistaminics or local vasoconstrictors, antazoline derivatives

<i>-azone (see -buzone)</i>	anti-inflammatory analgesics, phenylbutazone derivatives
<i>-azosin</i>	antihypertensive substances, prazosin derivatives
<i>-bacept (see -cept)</i>	B-cell activating factor receptors
<i>-bactam</i>	β -lactamase inhibitors
<i>-bamate</i>	tranquillizers, propanediol and pentanediol derivatives
<i>barb</i>	hypnotics, barbituric acid derivatives
<i>-begron</i>	β_3 -adrenoreceptor agonists
<i>-benakin (see -kin)</i>	interleukin-1 analogues and derivatives
<i>-bendan (see -dan)</i>	cardiac stimulants, pimobendan derivatives
<i>-bendazole</i>	anthelmintics, tiabendazole derivatives
<i>-bercept (see -cept)</i>	target: VEGF receptors
<i>-bermin (see -ermin)</i>	vascular endothelial growth factors
<i>-bersat</i>	anticonvulsants, benzoylamino-benzpyran derivatives
<i>-betasol (see pred)</i>	prednisone and prednisolone derivatives
<i>bol</i>	anabolic steroids
<i>-bradine</i>	bradycardic agents
<i>-brate (see -fibrate)</i>	clofibrate derivatives
<i>-bufen</i>	non-steroidal anti-inflammatory agents, arylbutanoic acid derivatives
<i>-bulin</i>	antineoplastics; mitotic inhibitor, tubulin binder
<i>-butazone (see -buzone)</i>	anti-inflammatory analgesics, phenylbutazone derivatives
<i>-buvir (see vir)</i>	RNA polymerase (NS5B) inhibitors
<i>-buzone</i>	anti-inflammatory analgesics, phenylbutazone derivatives
<i>-caine</i>	local anaesthetics
<i>-cain-</i>	class I antiarrhythmics, procainamide and lidocaine derivatives
<i>calci</i>	vitamin D analogues/derivatives

<i>-capone</i>	catechol- <i>O</i> -methyltransferase (COMT) inhibitors
<i>carbef</i>	antibiotics, carbacephem derivatives
<i>-carnil (see -azenil)</i>	benzodiazepine receptor antagonists/agonists (carboline derivatives)
<i>-castat (see -stat)</i>	dopamine-hydroxylase inhibitors
<i>-cavir (see vir)</i>	carbocyclic nucleosides
<i>cef-</i>	antibiotics, cephalosporanic acid derivatives
<i>cell-/cel-</i>	cellulose derivatives
<i>-cel</i>	cell therapy products
<i>cell-ate (see cell-/cel-)</i>	cellulose ester derivatives for substances containing acidic residues
<i>-cellose (see cell-/cel-)</i>	cellulose ether derivatives
<i>-cept</i>	receptor molecules, native or modified (a preceding infix should designate the target)
<i>-cic</i>	hepatoprotective substances with a carboxylic acid group
<i>-ciclib</i>	cyclin dependant kinase inhibitors
<i>-ciclovir (see vir)</i>	antivirals, bicyclic heterocycles compounds
<i>-cidin</i>	naturally occurring antibiotics (undefined group)
<i>-ciguat</i>	guanylate cyclase activators and stimulators
<i>-cillide (see -cillin)</i>	antibiotics, 6-aminopenicillanic acid derivatives
<i>-cillin</i>	antibiotics, 6-aminopenicillanic acid derivatives
<i>-cillinam (see -cillin)</i>	antibiotics, 6-aminopenicillanic acid derivatives
<i>-cilpine (see -pine)</i>	tricyclic compounds
<i>-cisteine (see -steine)</i>	mucoytics, other than bromhexine derivatives
<i>-citabine</i>	nucleosides antiviral or antineoplastic agents, cytarabine or azacitidine derivatives
<i>-citinib (see -tinib)</i>	Janus kinase inhibitors, antineoplastics
<i>-clidine/-clidinium</i>	muscarinic receptor agonists/antagonists

<i>-clone</i>	hypnotic tranquillizers
<i>-cocept (see -cept)</i>	complement receptors
<i>-cog</i>	blood coagulation factors
<i>-cogin</i>	blood coagulation cascade inhibitors
<i>-conazole</i>	systemic antifungal agents, miconazole derivatives
<i>cort</i>	corticosteroids, except prednisolone derivatives
<i>-coxib</i>	selective cyclo-oxygenase inhibitors
<i>-crinat</i>	diuretics, etacrynic acid derivatives
<i>-crine</i>	acridine derivatives
<i>-cromil</i>	antiallergics, cromoglicic acid derivatives
<i>-curium (see -ium)</i>	curare-like substances
<i>-cycline</i>	antibiotics, protein-synthesis inhibitors, tetracycline derivatives
<i>-dan</i>	cardiac stimulants, pimobendan derivatives
<i>-dapson</i>	antimycobacterials, diaminodiphenylsulfone derivatives
<i>-decakin (see -kin)</i>	interleukin-10 analogues and derivatives
<i>-degib</i>	SMO receptor antagonists
<i>-denoson</i>	adenosine A receptor agonists
<i>-dermin (see -ermin)</i>	epidermal growth factors
<i>-dil</i>	vasodilators
<i>-dilol (see -dil)</i>	vasodilators
<i>-dipine</i>	calcium channel blockers, nifedipine derivatives
<i>-dismase (see -ase)</i>	enzymes with superoxide dismutase activity, see <i>-ase</i> item V
<i>-distim (see -stim)</i>	combination of two different types of colony stimulating factors
<i>-dodekin (see -kin)</i>	interleukin-12 analogues and derivatives

<i>-dopa</i>	dopamine receptor agonists, dopamine derivatives, used as antiparkinsonism/prolactin inhibitors
<i>-dox (see -ox/-alox)</i>	antibacterials, quinazoline dioxide derivatives
<i>-dotin</i>	synthetic derivatives of dolastatin series
<i>-dotril (see -tril/trilat)</i>	endopeptidase inhibitors
<i>-dox (see -ox/-alox)</i>	antacids, aluminium derivatives (see also <i>-aldrate</i>)
<i>-dralazine</i>	antihypertensives, hydrazinephthalazine derivatives
<i>-drine</i>	sympathomimetics
<i>-dronic acid</i>	calcium metabolism regulator, pharmaceutical aid
<i>-dutant (see -tant)</i>	neurokinin NK ₂ receptor antagonist
<i>-dyl (see -dil)</i>	vasodilators
<i>-ectin</i>	antiparasitics, ivermectin derivatives
<i>-elestat (see -stat)</i>	elastase inhibitors
<i>-elvekin (see -kin)</i>	interleukin-11 analogues and derivatives
<i>-emcinal</i>	erythromycin derivatives lacking antibiotic activity, motilin agonists
<i>-enicokin (see -kin)</i>	interleukin-21 human analogues and derivatives
<i>-entan</i>	endothelin receptor antagonists
<i>(-)-eptacog (see -cog)</i>	blood coagulation VII
<i>erg</i>	ergot alkaloid derivatives
<i>-eridine</i>	analgesics, pethidine derivatives
<i>-ermin</i>	growth factors
<i>estr</i>	estrogens
<i>-etanide (see -anide)</i>	diuretics, piretanide derivatives
<i>-ethidine (see -eridine)</i>	analgesics, pethidine derivatives
<i>-exakin (see -kin)</i>	interleukin-6 analogues and derivatives

<i>-exine</i>	mucoytic, bromhexine derivatives
<i>-farcept (see -cept)</i>	subgroup of interferon receptors
<i>-fenamate</i> (<i>see -fenamic acid</i>)	"fenamic acid" derivatives
<i>-fenacin</i>	muscarinic receptor antagonists
<i>-fenamic acid</i>	anti-inflammatory, anthranilic acid derivatives
<i>-fenin</i>	diagnostic aids; (phenylcarbamoyl)methyl iminodiacetic acid derivatives
<i>-fenine</i>	analgesics, glafenine derivatives (subgroup of fenamic acid group)
<i>-fensine</i>	norepinephrine, serotonin, dopamine reuptake inhibitors
<i>-fentanil</i>	opioid receptor agonists, analgesics, fentanyl derivatives
<i>-fentrine</i>	inhibitors of phosphodiesterases
<i>-fermin (see -ermin)</i>	fibroblast growth factors
<i>-fiban</i>	fibrinogen receptor antagonists (glycoprotein IIb/IIIa receptor antagonists)
<i>-fibrate</i>	clofibrate derivatives
<i>-filermin (see -ermin)</i>	leukemia-inhibiting factor
<i>-flapon</i>	5-lipoxygenase-activating protein (FLAP) inhibitor
<i>-flurane</i>	halogenated compounds used as general inhalation anaesthetics
<i>-formin</i>	antihyperglycaemics, phenformin derivatives
<i>fos</i>	insecticides, anthelmintics, pesticides etc., phosphorous derivatives
<i>-fosfamide (see -fos)</i>	alkylating agents of the cyclophosphamide group
<i>-fosine (see -fos)</i>	cytostatic
<i>-fovir (see vir)</i>	phosphonic acid derivatives
<i>-fradil</i>	calcium channel blockers acting as vasodilators
<i>-frine (see -drine)</i>	sympathomimetic, phenethyl derivatives
<i>-fungin</i>	antifungal antibiotics

<i>-fylline</i>	N-methylated xanthine derivatives
<i>gab</i>	gabamimetic agents
<i>gado-</i>	diagnostic agents, gadolinium derivatives
<i>-gattran</i>	thrombin inhibitor, antithrombotic agent
<i>-gene</i>	gene therapy products
<i>gest</i>	steroids, progestogens
<i>-gestr- (see estr)</i>	estrogens
<i>-giline</i>	monoamine oxydase (MAO)-inhibitors type B
<i>-gillin</i>	antibiotics produced by <i>Aspergillus</i> strains
<i>gli</i>	antihyperglycaemics
<i>-gliflozin (see gli)</i>	sodium glucose co-transporter inhibitors, phlorizin derivatives
<i>-gliptin (see gli)</i>	dipeptidyl aminopeptidase–IV inhibitors
<i>-glitazar (see gli)</i>	peroxisome proliferator activating receptor- γ (PPAR- γ) agonists
<i>-glitazone (see gli)</i>	peroxisome proliferator activating receptor- γ (PPAR- γ) agonists, thiazolidinedione derivatives
<i>-glumide</i>	cholecystokinin (CCK) antagonists, antiulcer, anxiolytic agent
<i>-glurant</i>	metabotropic glutamate receptor antagonists / negative allosteric modulators
<i>-glutide (see -tide)</i>	Glucagon-Like Peptide (GLP) analogues
<i>-golide</i>	dopamine receptor agonists, ergoline derivatives
<i>-gosivir (see vir)</i>	glucoside inhibitors
<i>-gramostim (see -stim)</i>	granulocyte macrophage colony stimulating factor (GM-CSF) types substances
<i>-grastim (see -stim)</i>	granulocyte colony stimulating factor (G-CSF) type substances
<i>-grel-/grel</i>	platelet aggregation inhibitors
<i>guan-</i>	antihypertensives, guanidine derivatives
<i>-ibine (see -ribine)</i>	ribofuranyl-derivatives of the “pyrazofurin” type

<i>-icam</i>	anti-inflammatory, isoxicam derivatives
<i>-ifene</i>	antiestrogens or estrogen receptor modulators, clomifene and tamoxifen derivatives
<i>-igetide (see -tide)</i>	peptides and glycopeptides
<i>-ilide</i>	class III antiarrhythmics, sematilide derivatives
<i>imex</i>	immunostimulants
<i>-imibe</i>	antihyperlipidaemics, acyl CoA: cholesterol acyltransferase (ACAT) inhibitors
<i>-imod</i>	immunomodulators, both stimulant/suppressive and stimulant
<i>-imus</i>	immunosuppressants (other than antineoplastics)
<i>-ine</i>	alkaloids and organic bases
<i>-inostat (see stat)</i>	histone deacetylase inhibitors
<i>io-</i>	iodine-containing contrast media
<i>iod-/io-</i>	iodine-containing compounds other than contrast media
<i>-irudin</i>	thrombin inhibitors, hirudin derivatives
<i>-isant</i>	histamine H ₃ receptor antagonists
<i>-isomide</i>	class I antiarrhythmics, disopyramide derivatives
<i>-ium</i>	quaternary ammonium compounds
<i>-izine (-yzine)</i>	diphenylmethyl piperazine derivatives
<i>-kacin</i>	antibiotics, kanamycin and bekanamycin derivatives (obtained from <i>Streptomyces kanamyceticus</i>)
<i>-kalant</i>	potassium channel blockers
<i>-kalim</i>	potassium channel activators, antihypertensive
<i>-kef-</i>	enkephalin agonists
<i>-kin</i>	interleukin type substances
<i>-ki(n)- (see -mab)</i>	target: interleukin

<i>-kinra (see -kin)</i>	interleukin receptor antagonists
<i>-kiren</i>	renin inhibitors
<i>-lefacept (see -cept)</i>	lymphocyte function-associated antigen 3 receptors
<i>-leukin (see -kin)</i>	interleukin-2 analogues and derivatives
<i>-lisib</i>	phosphatidylinositol 3-kinase inhibitors, antineoplastics
<i>-listat (see -stat)</i>	gastrointestinal lipase inhibitors
<i>-lubant</i>	leukotriene B ₄ receptor antagonist
<i>-lukast (see -ast)</i>	leukotriene receptor antagonists
<i>-lutamide</i>	non-steroid antiandrogens
<i>-lutril (see -tril/trilat)</i>	endopeptidase inhibitors
<i>-mab</i>	monoclonal antibodies
<i>-mantadine</i>	adamantane derivatives
<i>-mantine (see -mantadine)</i>	adamantane derivatives
<i>-mantone (see -mantadine)</i>	adamantane derivatives
<i>-mapimod (see -imod)</i>	mitogen-activated protein (MAP) kinase inhibitors
<i>-mastat (see -stat)</i>	matrix metalloproteinase inhibitors
<i>-meline</i>	cholinergic agents (muscarine receptor agonists/partial antagonists used in the treatment of Alzheimer's disease)
<i>mer-/-mer</i>	mercury-containing drugs, antimicrobial or diuretic
<i>-mer</i>	polymers
<i>-mesine</i>	sigma receptor ligands
<i>-mestane</i>	aromatase inhibitors
<i>-metacin</i>	anti-inflammatory, indometacin derivatives
<i>-met(h)asone (see pred)</i>	prednisone and prednisolone derivatives

<i>-metinib (see -tinib)</i>	MEK (MAPK kinase) tyrosine kinase inhibitors
<i>-micin</i>	aminoglycosides, antibiotics obtained from various <i>Micromonospora</i>
<i>-mifene (see -ifene)</i>	antiestrogens, clomifene and tamoxifen derivatives
<i>-milast (see -ast)</i>	phosphodiesterase IV (PDE IV) inhibitors
<i>mito-</i>	antineoplastics, nucleotoxic agents
<i>-monam</i>	monobactam antibiotics
<i>-morelin (see -relin)</i>	growth hormone release-stimulating peptides
<i>-mostat (see -stat)</i>	proteolytic enzyme inhibitors
<i>-mostim (see -stim)</i>	macrophage stimulating factors (M-CSF) type substances
<i>-motide (see -tide)</i>	immunological agents for active immunization
<i>-motine</i>	antivirals, quinoline derivatives
<i>-moxin</i>	monoamine oxidase inhibitors, hydrazine derivatives
<i>-mulin</i>	antibacterials, pleuromulin derivatives
<i>-mustine</i>	antineoplastic, alkylating agents, (β -chloroethyl)amine derivatives
<i>-mycin</i>	antibiotics, produced by <i>Streptomyces</i> strains (see also <i>-kacin</i>)
<i>nab</i>	cannabinoid receptors agonists
<i>-nabant</i>	cannabinoid receptors antagonists
<i>-nacept (see -cept)</i>	interleukin-1 receptors
<i>-nakin (see -kin)</i>	interleukin-1 analogues and derivatives
<i>-nakinra (see -kin)</i>	interleukin-1 receptor antagonists
<i>nal-</i>	opioid receptor antagonists/agonists related to normorphine
<i>-naritide (see -tide)</i>	peptides and glycopeptides
<i>-navir (see vir)</i>	Human Immunodeficiency Virus (HIV) protease inhibitors
<i>-nepag</i>	prostaglandins receptors agonists, non-prostanoids
<i>-nermin (see -ermin)</i>	tumour necrosis factor

<i>-nercept (see -cept)</i>	tumour necrosis factor receptors
<i>-nertant (see -tant)</i>	neurotensin antagonists
<i>-netant (see -tant)</i>	neurokinin NK ₃ receptor antagonists
<i>-nicate (see nico-)</i>	antihypercholesterolaemic and/or vasodilating nicotinic acid esters
<i>-nicline</i>	nicotinic acetylcholine receptor partial agonists / agonists
<i>nico-/nic-/ni-</i>	nicotinic acid or nicotinoyl alcohol derivatives
<i>-nidazole</i>	antiprotozoals and radiosensitizers, metronidazole derivatives
<i>-nidine (see -onidine)</i>	antihypertensives, clonidine derivatives
<i>nifur-</i>	5-nitrofurans derivatives
<i>-nil (see -azenil)</i>	benzodiazepine receptor antagonists/agonists (benzodiazepine derivatives)
<i>nitro-/nitr-/nit-/ni-/ni-</i>	NO ₂ – derivatives
<i>-nixin</i>	anti-inflammatory, anilonicotinic acid derivatives
<i>(-)nonacog (see -cog)</i>	blood factor IX
<i>octakin (see -kin)</i>	interleukin-8 analogues and derivatives
<i>-octadekin (see -kin)</i>	interleukin-18 human analogues and derivatives
<i>(-)octocog (see -cog)</i>	blood factor VIII
<i>-ol</i>	for alcohols and phenols
<i>-olol</i>	β-adrenoreceptor antagonists
<i>-olone (see pred)</i>	steroids other than prednisolone derivatives
<i>-onakin (see -kin)</i>	interleukin-1 analogues and derivatives
<i>-one</i>	ketones
<i>-onide</i>	steroids for topical use, acetal derivatives
<i>-onidine</i>	antihypertensives, clonidine derivatives
<i>-onium (see -ium)</i>	quaternary ammonium compounds

<i>-opamine (see -dopa)</i>	dopaminergic agents dopamine derivatives used as cardiac stimulant/antihypertensives/diuretics
<i>-orex</i>	anorexics
<i>-orph- (see orphan)</i>	opioid receptor antagonists/agonists, morphinan derivatives
<i>orphan</i>	opioid receptor antagonists/agonists, morphinan derivatives
<i>-otermin (see -ermin)</i>	bone morphogenetic proteins
<i>-ox/-alox</i>	antacids, aluminium derivatives
<i>-oxacin</i>	antibacterials, nalidixic acid derivatives
<i>-oxan(e)</i>	benzodioxane derivatives
<i>-oxanide (see -anide)</i>	antiparasitics, salicylanilides and analogues
<i>-oxef (see cef-)</i>	antibiotics, oxacefalosporanic acid derivatives
<i>-oxepin (see -pine)</i>	tricyclic compounds
<i>-oxetine</i>	serotonin and/or norepinephrine reuptake inhibitors, fluoxetine derivatives
<i>-oxicam (see -icam)</i>	anti-inflammatory, isoxicam derivatives
<i>-oxifene (see -ifene)</i>	antiestrogens or estrogen receptor modulators, clomifene and tamoxifen derivatives
<i>-oxopine (see -pine)</i>	tricyclic compounds
<i>-pafant</i>	platelet-activating factor antagonists
<i>-pamide</i>	diuretics, sulfamoylbenzoic acid derivatives (could be sulfamoylbenzamide)
<i>-pamil</i>	calcium channel blocker, verapamil derivatives
<i>-parcin</i>	for glycopeptide antibiotics
<i>-parib</i>	poly-ADP-ribose polymerase inhibitors
<i>-parin</i>	heparin derivatives including low molecular mass heparins
<i>-parinux (see -parin)</i>	synthetic heparinoids
<i>-pendyl (see -dil)</i>	vasodilators

<i>-penem</i>	analogues of penicillanic acid antibiotics modified in the five-membered ring
<i>perfl(u)-</i>	perfluorinated compounds used as blood substitutes and/or diagnostic agents
<i>-peridol (see -perone)</i>	antipsychotics, haloperidol derivatives
<i>-peridone (see -perone)</i>	antipsychotics, risperidone derivatives
<i>-perone</i>	tranquillizers, neuroleptics, 4'-fluoro-4-piperidinobutyrophenone derivatives
<i>-pidem</i>	hypnotics/sedatives, zolpidem derivatives
<i>-pin(e)</i>	tricyclic compounds
<i>-piprant</i>	prostaglandin receptors antagonists, non-prostanoids
<i>-piprazole (see -prazole)</i>	psychotropics, phenylpiperazine derivatives
<i>-pirone (see -spirone)</i>	anxiolytics, buspirone derivatives
<i>-pirox (see -ox/-alox)</i>	antimycotic pyridone derivatives
<i>-pitant (see -tant)</i>	neurokinin NK ₁ (substance P) receptor antagonist
<i>-plact</i>	platelet factor 4 analogues and derivatives
<i>-pladib</i>	phospholipase A ₂ inhibitors
<i>-planin</i>	glycopeptide antibacterials (<i>Actinoplanes</i> strains)
<i>-plase (see -ase)</i>	enzymes
<i>-plasmid (see -gene)</i>	gene therapy products
<i>-platin</i>	antineoplastic agents, platinum derivatives
<i>-plermin (see -ermin)</i>	platelet-derived growth factor
<i>-plestim (see -stim and -kin)</i>	interleukin-3 analogues and derivatives
<i>-plon</i>	imidazopyrimidine or pyrazolopyrimidine derivatives, used as anxiolytics, sedatives, hypnotics
<i>-poetin</i>	erythropoietin type blood factors

<i>-porfin</i>	benzoporphyrin derivatives
<i>-poride</i>	Na ⁺ /H ⁺ antiport inhibitor
<i>-pramine</i>	substances of the imipramine group
<i>-prazole</i>	antiulcer, benzimidazole derivatives
<i>-piprazole</i>	psychotropics, phenylpiperazine derivatives
<i>-prazan</i>	proton pump inhibitors, not dependent on acid activation
<i>pred</i>	prednisone and prednisolone derivatives
<i>-prenaline (see -terol)</i>	bronchodilators, phenethylamine derivatives
<i>-pressin</i>	vasoconstrictors, vasopressin derivatives
<i>-previr (see vir)</i>	Hepatitis Virus C (HVC) protease inhibitors
<i>-pride</i>	sulpiride derivatives
<i>-pril</i>	angiotensin-converting enzyme inhibitors
<i>-prilat (see -pril)</i>	angiotensin-converting enzyme inhibitors
<i>-prim</i>	antibacterials, dihydrofolate reductase (DHFR) inhibitors, trimethoprim derivatives
<i>-pris-</i>	steroidal compounds acting on progesterone receptors (excluding <i>-gest-</i> compounds)
<i>-pristin</i>	antibacterials, streptogramins, protein synthesis inhibitors, pristinamycin derivatives
<i>-profen</i>	anti-inflammatory agents, ibuprofen derivatives
<i>prost</i>	prostaglandins
<i>-prostil (see prost)</i>	prostaglandins, anti-ulcer
<i>-quidar</i>	drugs used in multidrug resistance, quinoline derivatives
<i>-quin(e)</i>	quinoline derivatives
<i>-quinil (see -azenil)</i>	benzodiazepine receptor agonists, also partial or inverse (quinoline derivatives)

<i>-racetam</i>	amide type nootrope agents, piracetam derivatives
<i>-racil</i>	uracil type antineoplastics
<i>-rafenib</i>	RAF (rapidly accelerated fibrosarcoma) kinase inhibitors
<i>-relin</i>	pituitary hormone-release stimulating peptides
<i>-relix</i>	gonadotropin-releasing-hormone (GnRH) inhibitors, peptides
<i>-renone</i>	aldosterone antagonists, spironolactone derivates
<i>-restat (see -stat)</i>	aldose reductase inhibitors
<i>retin</i>	retinol derivatives
<i>-ribine</i>	ribofuranyl-derivatives of the "pyrazofurin" type
<i>rifa-</i>	antibiotics, rifamycin derivatives
<i>-rinone</i>	cardiac stimulants, amrinone derivatives
<i>-ritide (see -tide)</i>	natriuretic peptides
<i>-rixin</i>	chemokine CXCR receptors antagonists
<i>-rizine (see -izine)</i>	antihistaminics/cerebral (or peripheral) vasodilators
<i>-rolimus (see -imus)</i>	immunosuppressants, rapamycin derivatives
<i>-rozole</i>	aromatase inhibitors, imidazole-triazole derivatives
<i>-rsen</i>	antisense oligonucleotides
<i>-rubicin</i>	antineoplastics, daunorubicin derivatives
<i>sal</i>	salicylic acid derivatives
<i>salazo-</i>	phenylazosalicylic acid derivatives antibacterial
<i>-salan</i>	brominated salicylamide derivatives disinfectant
<i>-sartan</i>	angiotensin II receptor antagonists, antihypertensive (non-peptidic)
<i>-semide</i>	diuretics, furosemide derivatives
<i>-sermin (see -ermin)</i>	insulin-like growth factors
<i>-serod</i>	serotonin receptor antagonists and partial agonists

<i>-serpine</i>	derivatives of <i>Rauwolfia</i> alkaloids
<i>-sertib</i>	serine/threonine kinase inhibitors
<i>-setron</i>	serotonin receptor antagonists (5-HT ₃) not fitting into other established groups of serotonin receptor antagonists
<i>-siran</i>	small interfering RNA
<i>som-</i>	growth hormone derivatives
<i>-sopine (see -pine)</i>	tricyclic compounds
<i>-spirone</i>	anxiolytics, buspirone derivatives
<i>-stat/-stat-</i>	enzyme inhibitors
<i>-steine</i>	mucolytics, other than bromhexine derivatives
<i>-ster-</i>	androgens/anabolic steroids
<i>-steride (see -ster-)</i>	androgens/anabolic steroids
<i>-stigmine</i>	acetylcholinesterase inhibitors
<i>-stim</i>	colony stimulating factors
<i>sulfa-</i>	anti-infectives, sulfonamides
<i>-sulfan</i>	antineoplastic, alkylating agents, methanesulfonates
<i>-tacept (see -cept)</i>	cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) receptors
<i>-tadine</i>	tricyclic histamine-H ₁ receptor antagonists, tricyclic compounds
<i>-tansine</i>	maytansinoid derivatives, antineoplastics
<i>-tant</i>	neurokinin (tachykinin) receptor antagonists
<i>-tapide</i>	microsomal triglyceride transfer protein (MTP) inhibitors
<i>-taxel</i>	antineoplastics; taxane derivatives
<i>-tecan</i>	antineoplastics, topoisomerase I inhibitors
<i>-tepa</i>	antineoplastics, thiotepa derivatives
<i>-tepine (see -pine)</i>	tricyclic compounds

<i>-teplase (see -ase)</i>	tissue type plasminogen activators, see <i>-ase</i> item VI
<i>-tercept (see -cept)</i>	transforming growth factors receptors
<i>-termin (see -ermin)</i>	transforming growth factor
<i>-terol</i>	bronchodilators, phenethylamine derivatives
<i>-terone</i>	antiandrogens
<i>-thiouracil (see -racil)</i>	uracil derivatives used as thyroid antagonists
<i>-tiazem</i>	calcium channel blockers, diltiazem derivatives
<i>-tibant</i>	bradykinin receptor antagonists
<i>-tide</i>	peptides and glycopeptides (for special groups of peptides see <i>-actide</i> , <i>-pressin</i> , <i>-relin</i> , <i>-tocin</i>)
<i>-tidine</i>	histamine-H ₂ -receptor antagonists, cimetidine derivatives
<i>-tilide (see -ilide)</i>	class III antiarrhythmics, sematilide derivatives
<i>-tiline (see -triptyline)</i>	antidepressants, dibenzo[a,d]cycloheptane or cycloheptene derivatives
<i>-tinib</i>	tyrosine kinase inhibitors
<i>-tirelin (see -relin)</i>	thyrotropin releasing hormone analogues
<i>-tizide</i>	diuretics, chlorothiazide derivatives
<i>-tocin</i>	oxytocin derivatives
<i>-toin</i>	antiepileptics, hydantoin derivatives
<i>-tolimod (see -imod)</i>	toll-like receptors (TLR) agonists
<i>-trakin (see -kin)</i>	interleukin-4 analogues and derivatives
<i>-trakinra (see -kinra)</i>	interleukin-4 receptor antagonists
<i>-traline</i>	serotonin reuptake inhibitors
<i>-tredekin (see -kin)</i>	interleukin-13 analogues and derivatives
<i>-trexate</i>	folic acid analogues
<i>-trexed</i>	antineoplastics; thymidilate synthetase inhibitors

<i>-tricin</i>	antibiotics, polyene derivatives
<i>-tril/trilat</i>	endopeptidase inhibitors
<i>-triptan</i>	serotonin (5-HT ₁) receptor agonists, sumatriptan derivatives
<i>-triptyline</i>	antidepressants, dibenzo[a,d]cycloheptane or cycloheptene derivatives
<i>-troban</i>	thromboxane A ₂ -receptor antagonists; antithrombotic agents
<i>-trodist (see -ast)</i>	thromboxane A ₂ -receptor antagonists, antiasthmatics
<i>trop</i>	atropine derivatives
<i>-uplase (see -ase)</i>	urokinase type plasminogen activator, see -ase item VII
<i>-ur (see -uridine)</i>	uridine derivatives used as antiviral agents and as antineoplastics
<i>-uridine</i>	uridine derivatives used as antiviral agents and as antineoplastics
<i>-vaptan</i>	vasopressin receptor antagonists
<i>-vastatin (see -stat)</i>	antihyperlipidaemic substances, HMG CoA reductase inhibitors
<i>-vec (see -gene)</i>	gene therapy product
<i>-verine</i>	spasmolytics with a papaverine-like action
<i>vin-/-vin-</i>	vinca alkaloids
<i>vir</i>	antivirals (undefined group)
<i>-vircept (see -cept)</i>	antiviral receptors
<i>-virine (see vir)</i>	non-nucleoside reverse transcriptase inhibitors (NNRTI)
<i>-viroc (see -vir)</i>	CCR5 (Chemokine CC motif receptor 5) receptor antagonists
<i>-virsen</i>	antisense oligonucleotides
<i>-vos (see fos)</i>	insecticides, anthelmintics, pesticides etc., phosphorus derivatives
<i>-vudine (see -uridine)</i>	uridine derivatives used as antiviral agents and as antineoplastics
<i>-xaban</i>	blood coagulation factor X _A inhibitors, antithrombotics
<i>-xanox (see -ox/-alox)</i>	anti-allergics, tixanox group
<i>-xetan</i>	chelating agents

-yzine (<i>see -izine</i>)	diphenylmethyl piperazine derivatives
-zafone	alozafone derivatives
-zepine (<i>see -pine</i>)	tricyclic compounds
-zolast (<i>see -ast</i>)	leukotriene biosynthesis inhibitors
-zomib	proteasome inhibitors
-zone (<i>see -buzone</i>)	anti-inflammatory analgesics, phenylbutazone derivatives
-zotan	5-HT _{1A} receptor agonists / antagonists acting primarily as neuroprotectors

Explanatory note.-

The hyphens indicate the position of the stem, prefix, infix or suffix, within the INN. In the event that the hyphen is absent, the stem may be used in any position within the name.

<i>STEM</i>	<i>DEFINITION</i>
mer-or -mer-	mercury-containing drugs, antimicrobial or diuretic (deleted from General Principles in List 28 prop. INN)
mito-	antineoplastics, nucleotoxic agents (deleted from General Principles in List 24 prop. INN)
-ol	alcohols and phenols (deleted from General Principles in 14th report)
-quine, quin	quinoline derivatives (deleted from General Principles in List 28 prop. INN)
-stigmine	anticholinesterases (deleted from General Principles in List 24 prop. INN)

Nomenclature of biological and biotechnological substances (a summary)

(For details and examples please see the document WHO/EMP/RHT/TSN/2016.1: International Nonproprietary Names (INN) for biological and biotechnological substances (a review)).

The nomenclature of biological and biotechnological substances is based on: General Policies, Stems and Schemes.

General Policies

The nomenclature of biological and biotechnological substances has some general policies for several groups of substances, yet not all groups have general policies. There are several biological groups whose policy is to not assign an INN. Examples of such groups are: natural blood products, immunoglobulins fractionated from plasma, skin substitutes and vaccines. The biological groups for which presently it exists clear general policies and for which an INN is assigned, are the following:

- non-glycosylated substances
- glycosylated substances
- fusion proteins
- pegylated substances
- cell therapies
- gene therapies
- monoclonal antibodies

Stems

The names of substances related by structure and/or function have specific letter groups, called stems. Most of biological substances are identified with a stem. Table 1 summarises all biological groups identified with a stem or a pre-stem, and Table 2 summarizes all biological substances that are not identified by a stem or pre-stem.

Table 1: Biological groups with respective stems.

Name of the group	Stem
Antimicrobial, bactericidal permeability increasing polypeptides	- <i>ganan</i> (pre-stem)
Antisense oligonucleotides	- <i>rsen</i>
Aptamers, classical and mirror ones	- <i>apt-</i>
Blood coagulation cascade inhibitors	- <i>cogin</i>

Blood coagulation factors	<i>-cog</i>
Cell therapies	<i>-cel</i>
Colony stimulating factors	<i>-stim</i>
Enzymes	<i>-ase</i>
Erythropoietin type blood factors	<i>-poetin</i>
Gene therapies	<i>-gene</i>
Gonadotropin-releasing hormone (GnRH) inhibiting peptides	<i>-relix</i>
Growth factors and Tumour necrosis factors (TNF)	<i>-ermin</i>
Growth hormone (GH) derivatives	<i>som-</i>
Heparin derivatives including low molecular mass heparins	<i>-parin</i>
Hirudin derivatives	<i>-irudin</i>
Immunomodulators, both stimulant/suppressive and stimulant	<i>-imod</i>
Interleukin receptor antagonists	<i>-kinra</i>
Interleukin type substances	<i>-kin</i>
Monoclonal antibodies	<i>-mab</i>
Oxytocin derivatives	<i>-tocin</i>
Peptides and glycopeptides	<i>-tide</i>
Pituitary hormone-release stimulating peptides	<i>-relin</i>
Receptor molecules, native or modified	<i>-cept</i>
Small interfering RNA	<i>-siran-</i>
Synthetic polypeptides with a corticotropin-like action	<i>-actide</i>
Vasoconstrictors, vasopressin derivatives	<i>-pressin</i>

Table 2: Groups without respective stems / pre-stems

Name of the group
Antithrombins
Growth hormone (GH) antagonists
Insulins
Interferons

Pituitary / placental glycoprotein hormones
Thrombomodulins
Toxins
Vaccine-like substances (eg. peptide vaccines, recombinant vaccines)

Schemes

Some biological groups besides a stem (or pre-stem) also have a scheme. Those groups are: cell therapies, gene therapies and monoclonal antibodies.

Scheme for cell therapies¹:

The INN-USAN harmonized nomenclature scheme for cell therapies is composed by:

Prefix	+	Infix 1	+	Infix 2	+	Suffix
<i>(random)</i>		(manipulation)		(cell type)		“- <i>cel</i> ”

Examples of cell therapies:

spanlecortemlocel (112)

Scheme for gene therapies¹:

The INN nomenclature scheme for gene therapies is a two-word scheme with the first word representing the gene component and the second word the vector component, as follows:

Word 1: *gene component*

Prefix	+	Infix	+	Suffix
<i>(random)</i>		(gene)		“-(<i>a vowel</i>) <i>genel</i> ”

Word 2: *vector component*

Prefix	+	Infix	+	Suffix
<i>(random)</i>		(viral vector)		“- <i>vec</i> ” “- <i>repvec</i> ”

Examples of gene therapies:

¹ For examples of infixes and further details, please see *the document WHO/EMP/RHT/TSN/2016.1: International Nonproprietary Names (INN) for biological and biotechnological substances (a review)*.

aglatimagene besadenovec (113), beperminogene perplasmid (95), pexastimogene devacirepvec (108)

Scheme for monoclonal antibodies¹ (under discussion)

The INN nomenclature scheme for monoclonal antibodies is composed by:

Prefix	+	Sustem A	+	Substem B	+	Suffix
<i>(random)</i>		<i>(target class)</i>		<i>(species)</i>		<i>“-mab”</i>

Examples of monoclonal antibodies:

begelomab (111), bezlotoxumab (107), enoticumab (107), lilotomab (112), pagibaximab (93), refanezumab (114), romosozumab (106), tamtuvatmab (114), trevogrumab (113)

¹ For a list of substems and further details, please see *the document WHO/EMP/RHT/TSN/2016.1: International Nonproprietary Names (INN) for biological and biotechnological substances (a review)*.

WHA46.19 Nonproprietary names for pharmaceutical substances

The Forty-sixth World Health Assembly,

Recalling resolution WHA31.32 on the importance of using nonproprietary names in establishing national drug formularies;

Noting the fundamental contribution of the WHO Programme on international nonproprietary names (INN) to effective communication in medicine, and the challenge inherent in maintaining the nomenclature as new substances are introduced into clinical use;

Acknowledging with satisfaction the increasing contribution of generic products to national drug markets in both developed and developing countries;

Noting the current trend to market products with the same active ingredient as, and intended to be clinically interchangeable with, a product currently on the market (multisource products) under trademarks or brand names derived from stems or other descriptors for international nonproprietary names nomenclature;

Recognizing that such use, particularly in respect of single-ingredient prescription drugs, may compromise the safety of patients by creating confusion in prescribing and dispensing medicines and by interfering with the orderly development of the nomenclature for international nonproprietary names;

Aware of the concern expressed by the International Conference of Drug Regulatory Authorities at its last meeting about the increasing use of pharmaceutical brand names that are very similar to or derived from international nonproprietary names;

Noting the recommendation made by the WHO Expert Committee on the Use of Essential Drugs, in its fifth report¹, on the need to discourage, as a matter of urgency, the use of trademarks that are derived from international nonproprietary names,

1. REQUESTS Member States:

- 1) to enact rules or regulations, as necessary, to ensure that international nonproprietary names (or the equivalent nationally approved generic names) used in the labelling and advertising of pharmaceutical products are always displayed prominently;
 - 2) to encourage manufacturers to rely on their corporate name and the international nonproprietary names, rather than on trademarks, to promote and market multisource products introduced after patent expiration;
 - 3) to develop policy guidelines on the use and protection of international nonproprietary names, and to discourage the use of names derived from INNs, and particularly names including established INN stems as trademarks;
2. CALLS ON the Director-General to intensify his consultations with governments and representatives of the pharmaceutical industry on ways of reducing to a minimum the problems arising from drug nomenclatures that may create confusion and jeopardize the safety of patients.

¹ WHO Technical Report Series, No. 825, 1992.

Procedure for the selection of international nonproprietary names for pharmaceutical substances

1. Proposals for recommended international nonproprietary names shall be submitted to the World Health Organization on the form provided therefore.
2. Such proposals shall be submitted by the Director-General of the World Health Organization to the members of the Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations designated for this purpose, for consideration in accordance with the "*General principles for guidance in devising International Nonproprietary Names*". The name used by the person discovering or first developing and marketing a pharmaceutical substance shall be accepted, unless there are compelling reasons to the contrary.
3. Subsequent to the examination provided for in article 2, the Director-General of the World Health Organization shall give notice that a proposed international nonproprietary name is being considered.
 - A. Such notice shall be given by publication in the *Chronicle of the World Health Organization*¹ and by letter to Member States and to national pharmacopoeia commissions or other bodies designated by Member States.
 - i. Notice may also be sent to specific persons known to be concerned with a name under consideration.
 - B. Such notice shall:
 - i. set forth the name under consideration;
 - ii. identify the person who submitted a proposal for naming the substance, if so requested by such person;
 - iii. identify the substance for which a name is being considered;
 - iv. set forth the time within which comments and objections will be received and the person and place to whom they should be directed;
 - v. state the authority under which the World Health Organization is acting and refer to these rules of procedure.
 - C. In forwarding the notice, the Director-General of the World Health Organization shall request that Member States take such steps as are necessary to prevent the acquisition of proprietary rights in the proposed name during the period it is under consideration by the World Health Organization.
4. Comments on the proposed name may be forwarded by any person to the World Health Organization within four months of the date of publication, under article 3, of the name in the *Chronicle of the World Health Organization*¹.
5. A formal objection to a proposed name may be filed by any interested person within four months of the date of publication, under article 3, of the name in the *Chronicle of the World Health Organization*¹.
 - A. Such objection shall:
 - i. identify the person objecting;
 - ii. state his interest in the name;
 - iii. set forth the reasons for his objection to the name proposed.
6. Where there is a formal objection under article 5, the World Health Organization may either reconsider the proposed name or use its good offices to attempt to obtain withdrawal of the objection. Without prejudice to the consideration by the World Health Organization of a substitute name or names, a name shall not be selected by the World Health Organization as a recommended international nonproprietary name while there exists a formal objection thereto filed under article 5 which has not been

¹ The title of this publication was changed to *WHO Chronicle* in January 1958. From 1987 onwards list of INN are published in *WHO Drug Information*

withdrawn.

7. Where no objection has been filed under article 5, or all objections previously filed have been withdrawn, the Director-General of the World Health Organization shall give notice in accordance with subsection A of article 3 that the name has been selected by the World Health Organization as a recommended international nonproprietary name.

8. In forwarding a recommended international nonproprietary name to Member States under article 7, the Director-General of the World Health Organization shall:

- A. request that it be recognized as the nonproprietary name for the substance; and
- B. request that Member States take such steps as are necessary to prevent the acquisition of proprietary rights in the name, including prohibiting registration of the name as a trademark or tradename.

ANNEX 7

 WORLD HEALTH ORGANIZATION	Request for an international nonproprietary name (INN) Demande de dénomination commune internationale (DCI) Fee: US\$ 12000 (for details see overleaf)
<p>Authority or manufacturer: <i>Autorité ou fabricant:</i></p> <p>Name of applicant / <i>nom du demandeur:</i> Name of responsible officer / <i>nom du responsable:</i> Address / <i>adresse:</i></p> <p>Telephone No./<i>No. de téléphone:</i> Fax No./<i>No. de fax</i> E-mail/<i>adresse électronique:</i></p> <p>We hereby request the World Health Organization to establish a free and unrestricted INN for the pharmaceutical substance described below. <i>L'OMS est priée de bien vouloir établir une DCI à usage libre pour la substance pharmaceutique en question.</i></p>	<p>For completion by WHO ▪ <i>A remplir par l'OMS</i></p> <p>Request No: Date: Copies forwarded:</p> <p>Date:</p> <p>Payment received: Date of cheque: Acknowledged:</p>
<p>SUGGESTED NAMES (in order of preference): <i>DENOMINATIONS PROPOSEES (par ordre de préférence)</i></p> <p>1..... 2..... 3.....</p> <p>CHEMICAL NAME OR DESCRIPTION (INCLUDING STEREOCHEMICAL INFORMATION): <i>NOM OU DESCRIPTION CHIMIQUE (Y COMPRIS L'INFORMATION SUR LA STÉRÉOCHIMIE)</i></p> <p>GRAPHIC FORMULA (INCLUDING AMINO ACID OR DNA SEQUENCES IN ELECTRONIC FORMAT) : <i>FORMULE GRAPHIQUE (Y COMPRIS LES SÉQUENCES D'ACIDES AMINÉS OU D'ADN EN FORMAT ÉLECTRONIQUE):</i></p> <p>MOLECULAR FORMULA: <i>FORMULE BRUTE</i></p> <p>CHEMICAL ABSTRACTS SERVICE (CAS) REGISTRY NUMBER: <i>NUMERO DU REGISTRE CAS</i></p> <p>TRADE NAME (known or contemplated): <i>NOM COMMERCIAL (connu ou envisagé)</i></p> <p>ANY OTHER NAME OR CODE: <i>AUTRE NOM OU CODE</i></p> <p>PRINCIPAL THERAPEUTIC USES AND POSOLOGY; PHARMACOLOGICAL ACTION: <i>UTILITE THÉRAPEUTIQUE ET POSOLOGIE; ACTION PHARMACOLOGIQUE</i></p>	

1. The process of selecting an INN should be initiated during that period of investigation when the compound is undergoing clinical study in human subjects. **Please indicate the date when clinical trials began:**

La procédure de sélection d'une DCI débute pendant la période d'investigation au cours de laquelle la substance fait l'objet d'études cliniques sur des sujets humains. Veuillez indiquer à quelle date ont débuté les essais cliniques:

2. This proposal is made on the understanding that insofar as is known, none of the suggested names is either registered or pending registration.

En présentant cette proposition, le signataire déclare qu'à sa connaissance aucune des dénominations suggérées n'a été déposée ou n'est sur le point de l'être.

3. Permission is granted to the WHO Secretariat to include a Chemical Abstract Name and registry number for the compound, its corresponding free acid, base or alcohol. **N.B.: A letter from Chemical Abstracts Service confirming the CAS Registry Number and the CA Index Name needs to be submitted by originators of requests together with the INN application form.**

L'autorisation est accordée à l'OMS, par la présente, d'inclure le nom et le numéro attribués par le Chemical Abstracts Service à la substance faisant l'objet de la demande ou à l'acide libre, base ou alcool correspondant. N.B.: Une lettre du Chemical Abstracts Service confirmant le numéro de registre du CAS et le nom du CAS doit être présentée par le requérant pour chaque demande de DCI en même temps que la soumission de la demande.

ADDITIONAL COMMENTS:

REMARQUES

Date

Signature

ADDITIONAL INFORMATION TO BE PROVIDED

Cell therapies:

- Name/Code designation
- Characterization/description
- Cell source
- List and description of manipulations (culture conditions included)
- If genetic manipulation: the detailed description of the vector and insert should be provided. If relevant, a separate gene therapy INN request should be submitted

Nucleic Acid-based substances: (e.g. oligonucleotides, gene therapies)

- The full nucleotide sequence of the substance in the following format: 50 nucleotides per line, in blocks of 10, with numbering at the end of each line (Word or in the text of an e-mail)
- The nucleotide sequence should be annotated to delineate relevant parts of the sequence (e.g. coding regions, control regions)
- A schematic map of the entire nucleic acid showing inserted/deleted gene(s) and relevant functional parts (not required for short oligonucleotides)

Pegylated substances:

- The details of pegylation: the end group and the polymer chain with the average number of repeat units (to 2 significant figures)
- The details of the linker (not the reagent used): where the linker is attached to the active moiety, and, ideally, if multiple sites are involved, in what proportion they are modified

Proteins and Peptides:

- The complete mature amino acid sequence in a format that can be copied for analysis (Word or in the text of an e-mail), using the single-letter code for each amino acid with spaces between groups of ten characters, five groups per line and with a number indicating the position of the last amino acid at the end of each line
- The positions of the disulfide bridges (at least a prediction) (for a monoclonal antibody: both, intra-chain and inter-chains) and all post-translational modifications listed after the amino acid sequence
- If available, the three dimensional structure in Protein Data Bank format or the Protein Data Bank accession code

Additional, for any recombinant DNA protein:

- The expression system (the cell type and the clone name used for the expression)
- The complete precursor nucleotide sequence with spaces between codons and translation (including the stop codon in 5') and with numbers per line, and in a format that can be copied for analysis (Word or in the text of an e-mail)
- If relevant, amino acid differences with the native sequence (for a monoclonal antibody: constant region amino acid changes by comparison with the closer genomic C gene and allele)

Additional, only for a glycoprotein/ glycopeptide:

The glycosylation profile (the types of sugar, the location of glycosylation site(s), etc.); if the cell line in which the protein/peptide is produced is engineered, detailed information if the glycosylation pattern is affected.

Additional, only for a conjugated protein:

The ratio: the mean numbers of molecules of the conjugated part (indicated by a range, thus integer numbers) per molecule of protein

Additional, only for a monoclonal antibody:

- IG class and subclass; IG format; species or Taxonomy Related structure (chimeric, humanized, synthetic construct); source (e.g., hybridoma, EBV immortalization, transgenic mice, phage display library) (for each chain, if different); CDR-IMGT (e.g., VH [8.7.11], V-KAPPA [12.3.9]) and the closer genomic (human or other species) V, J and C genes and alleles.
- Name/structure of the antigen against which the monoclonal antibody is directed
- Laboratory code name(s)
- If the terminal lysine is absent in the heavy chain amino acid sequence, a statement of the fabricant confirming that indeed there is no lysine codon in the nucleotide sequence (if not the lysine should be added in the amino acid sequence mentioning the post-translational modification clipping)

Please be aware that sequence information will be published either electronically (Mednet) or in both print and electronic format, depending on the size of the structure.

Examples can be found in published INN lists:

<http://www.who.int/medicines/publications/druginformation/innlists/en/>

The processing of a request for an International Nonproprietary Name (INN) is subject to the payment of a fixed fee of

US\$ 12000. (No other currency is accepted). Payment by bank transfer or by bankers certified cheque must be included with each request and should be made payable by:

Bank transfer: UBS AG
C.P. 2600
CH - 1211 Geneva 2, Switzerland
USD Account: 240 C0 169 920 3
USD Account IBAN: CH31 0024 0240 C01699203
Swift code: UBSWCHZH80A

Please send a copy of the bank transfer by fax to INN (0041 22 791 48 56), which will enable us to timely validate receipt of your payment.

Cheque payable to: World Health Organization
Avenue Appia
CH-1211 Geneva 27
Switzerland

To avoid delays in processing, the accompanying cheque should be sent by regular mail or special delivery to the INN programme, c/o Quality Assurance & Safety: Medicines (HSS/EMP) at the above address.

PLEASE ENSURE OUR REFERENCE NUMBER IS QUOTED ON PAYMENT:

EDM/INN26FT01000022

No request for an INN will be processed without payment having been received by WHO.

This request form must be completed and sent to the WHO INN Secretariat both in hard copy and electronic format.



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World Health Organization

International Nonproprietary Name (INN) Programme - innprogramme@who.int
RHT / TSN Technologies Standards and Norms - Department of Essential Medicines and Health Products (EMP) - Health Systems and Innovation (HIS) Cluster