

**International Nonproprietary Names (INN)
for biological and biotechnological substances**

(a review)

2019



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International Nonproprietary Names (INN) Programme

**Technologies Standards and Norms (TSN)
Regulation of Medicines and other Health Technologies (RHT)
Essential Medicines and Health Products (EMP)**

International Nonproprietary Names (INN) for biological and biotechnological substances

(a review)

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INTRODUCTION

More than 50 years ago, WHO established the International Nonproprietary Name (INN) Expert Group/WHO Expert Committee on Specifications for Pharmaceutical Preparations, to assign nonproprietary names to medicinal substances, so that each substance would be recognized globally by a unique name. These INNs do not give proprietary rights, unlike a trade mark, and can be used freely as they are public property.

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 names of compounds related by structure and/or function, specific letter groups, called stems, are included to aid recognition by health professionals. The *-actide* for synthetic polypeptides with a corticotrophin-like action is an early example.

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 anti-tumour, immunomodulatory 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 blood products, transgenic substances (human proteins expressed in animals or plants), substances for gene and cell therapy and novel vaccines.

As this area became more and more complex and challenging, the INN Expert Group requested the WHO-INN Secretariat to prepare a working document intended to summarize and review the past and present INN activities and policies in this field.

This document, first published on the website of the INN Programme in 2006, presents an inventory of the policy decisions taken by the INN Expert Group during these years of

change, and of the names assigned to biological and biotechnological substances. Considering the potential for further developments in the field of biologicals, this review is intended to be a living document which is updated regularly to include new policies and INN that have been assigned. The current version has been revised fully to reflect discussions and decisions taken by the INN Expert Group following a comprehensive review undertaken by many experts in the field, the INN Expert Group and INN Secretariat.

Comments and suggestions from all interested parties are always welcome and will be presented to the INN Expert Group for their consideration and for possible incorporation in future updates of this review.

You are reading the current updated version, also available as pdf-copy at:

<http://www.who.int/medicines/services/inn/publication/en/index.html>.

1. CURRENT STATUS OF EXISTING STEMS OR SYSTEMS FOR BIOLOGICAL AND BIOTECHNOLOGICAL SUBSTANCES [1-7]

1.1. Groups with their stems

Name of the group	Stem
Antimicrobial, bactericidal permeability increasing polypeptides (see item 3.1)	- <i>ganan</i> (pre-stem)
Antisense oligonucleotides (see item 3.2)	- <i>rse</i>
Aptamers, classical and mirror ones (see item 3.4)	- <i>apt-</i>
Blood coagulation cascade inhibitors (see item 3.5)	- <i>cogin</i>
Blood coagulation factors (see item 3.6)	- <i>cog</i>
Colony stimulating factors (see item 3.11)	- <i>stim</i>
Enzymes (see item 3.12)	- <i>ase</i>
Erythropoietin type blood factors (see item 3.13)	- <i>poetin</i>
Gonadotropin-releasing hormone (GnRH) inhibiting peptides (see item 3.15)	- <i>relix</i>
Growth factors and tumour necrosis factors (TNF) (see item 3.16)	- <i>ermin</i>
Growth hormone (GH) derivatives (see item 3.17)	<i>som-</i>
Heparin derivatives including low molecular weight heparins (see item 3.19)	- <i>parin</i>
Hirudin derivatives (see item 3.20)	- <i>irudin</i>
Immunomodulators, both stimulant/suppressive and stimulant (see item 3.21)	- <i>imod</i>
Interleukin receptor antagonists (see item 3.24)	- <i>kinra</i>
Interleukin type substances (see item 3.25)	- <i>kin</i>
Monoclonal antibodies (see items 2.9 and 3.26)	- <i>mab</i>
Oxytocin derivatives (see item 3.27)	- <i>tocin</i>
Peptides and glycopeptides (see item 3.28)	- <i>tide</i>
Pituitary hormone-release stimulating peptides (see item 3.29)	- <i>relin</i>
Receptor molecules, native or modified (see item 3.31)	- <i>cept</i>
Small interfering RNAs (see item 3.32)	- <i>siran-</i>
Substances for cell therapy (see items 2.6 and 3.8)	- <i>cel</i>
Substances for cell-based gene therapy (see items 2.7 and 3.9)	- <i>gene & -cel</i>
Substances for gene therapy (see items 2.5 and 3.7)	- <i>gene</i>
Synthetic polypeptides with a corticotropin-like action (see item 3.33)	- <i>actide</i>
Vasoconstrictors, vasopressin derivatives (see item 3.36)	- <i>pressin</i>

Substances for virus-based therapy (see items 2.8 and 3.10)	-rev
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1.2. Groups with INN nomenclature schemes

Name of the group
Fusion proteins with more than one pharmacological active component (see items 2.3 and 3.14)
Monoclonal antibodies (see items 2.9 and 3.26)
Substances for cell therapy (see items 2.6 and 3.8)
Substances for cell-based gene therapy (see items 2.7 and 3.9)
Substances for gene therapy (see items 2.5 and 3.7)
Substances for virus-based therapy (see items 2.8 and 3.10)

1.3. Groups without stems / pre-stems

Name of the group
Antithrombins (see item 3.3)
Growth hormone (GH) antagonists (see item 3.18)
Insulins (see item 3.22)
Interferons (see item 3.23)
Pituitary / placental glycoprotein hormones (see item 3.29)
Thrombomodulins (see item 3.34)
Toxins (see item 3.35)
Vaccine-like substances (eg. peptide vaccines, recombinant vaccines) (see items 2.14 and 3.37)

2. GENERAL POLICIES FOR BIOLOGICAL AND BIOTECHNOLOGICAL SUBSTANCES

2.1. General policy for non-glycosylated substances [8]

- For groups identified with a stem (e.g. *-irudin* for hirudin analogues) differences in the amino acid sequence are indicated by using a random prefix (e.g. *bivalirudin* (72)).
- For groups identified with a word (e.g. *insulin*) differences in the amino acid sequence are indicated by using a second element (e.g. *insulin argine* (58)).

2.2. General policy for glycosylated substances [8]

For groups of glycoproteins/glycopeptides identified with a stem (such as *-poetin* for erythropoetins, *-cog* for blood coagulation factors, *-ase* for enzymes...):

- differences in amino acid sequence in the same stem are indicated by using a random prefix (e.g. *rizolipase* (22), *burlulipase* (107));
- glycosylation is indicated by a Greek letter¹ spelt in full and added as a second word to the name. The Greek letters are used in the Greek alphabetical order starting from “*alfa*” (see ANNEX 4) (e.g. *epoetin alfa* (66), *eptacog alfa* (activated), *aglucoasidase alfa* (91), *epoetin beta* (62)).

For *-mab* and *-cept*:

Although most monoclonal antibodies (*-mab*) (see items 2.9 and 3.26) and receptor molecules (*-cept*) (see item 3.31) are glycosylated, the first INN application does not have the Greek letter (note however that it is considered “*alfa*”, despite not having “*alfa*” in its INN). If an INN application is received for a *-mab* or for a *-cept* with the same amino acid sequence as an existing one, but with differences in the glycosylation pattern requiring a new INN (eg. glycoengineering or having a cell-type glycosylation profile different from the existing application), the INN for the later application will be the existing INN, but with a terminal Greek letter, starting from “*beta*”.

For interferons:

In the case of interferons (see item 3.23), different glycosylation pattern is indicated by a small letter. The Greek letter identifies the subgroup.

¹ The transliteration of Greek letters in English, French and Spanish is given in ANNEX 4.

2.3. General policies for fusion proteins [4]

Fusion proteins are those encoded from one nucleotide sequence generated from two or more genes - and possibly linkers - that originally encoded separate proteins.

2.3.1. Fusion proteins with one pharmacologically active component²

- If a stem exists for the pharmacologically active component, this stem should be brought into the name.
- It is considered unnecessary to indicate that the substance is a fusion protein within the name.
- The prefix *alb-* has been used to designate proteins fused with human serum albumin and from proposed INN List 109, the prefix *ef-* has been used to designate proteins fused with the constant fragment of an immunoglobulin molecule (Fc), except for the *-cept* group.

2.3.2. Fusion proteins with more than one pharmacologically active component

- The stem *-fusp* is used to designate fusion proteins that contain more than one pharmacologically active components (e.g. action and targeting); no other stem is used.
- In addition to the stem *-fusp*, a syllable formed from a one consonant and one vowel is added before the stem to indicate: (a) consonant – the pharmaceutical action; and (b) vowel – the targeting, when appropriate. The meanings of these infix letters are given in Table 1.
- The stem *-fusp* has been used from proposed INN List 118. This nomenclature scheme is not designed to provide comprehensive information about the substance in the name, but rather to indicate that it is a fusion protein with more than one pharmacologically active component and a general indication of its type. The description at the level of publication provides information about the content of the fusion protein.
- In a bifunctional fusion protein, if one component has a purely stabilizing function (e.g. to increase half-life), the stem *-fusp* will not be assigned. For instance, if the component is a stabilizing Fc fragment, the “*ef-*” prefix should be used, not the stem *-fusp*.
In a fusion protein that contains one or more targeting components, one or more pharmacologically active components and also a stabilizing Fc fragment, both *-fusp* and *-ef* could be used.
- If both components of the fusion protein have a targeting action, and one of them is derived from a monoclonal antibody (mAb) or from a mAb fragment, when assigning the identifying infix letters, the “*-a-*” for *antibody* takes priority. For instance, a fusion of a

² The list of INN for fusion proteins with one pharmacologically active component is given in ANNEX 1.

receptor with an antibody will be *-ra-* (where *r* stands for *receptor* and *a* for *antibody*) not *-be-* (where *b* stands for *binding protein* and *e* for *receptor*).

- The infix letters will not distinguish between mAb or mAb fragments, in all these cases the letter “*a*” will be selected.
- Multiple mAb or mAb fragments will be named using the *-mab* nomenclature scheme, not the *-fusp* scheme.
- If more than two components are present, the two infix letters will still be used to represent the different action/targeting by class: e.g. if a fusion protein comprises two mAbs and one receptor, the INN will end in *-rafusp*.

Table 1: Infix letters and their meaning for the *-fusp* nomenclature scheme.

Action		Targeting	
<i>-b-</i>	binding protein	<i>-a-</i>	antibody
<i>-c-</i>	encapsulation protein	<i>-e-</i>	receptor
<i>-f-</i>	hormone	<i>-i-</i>	antigen
<i>-g-</i>	antigen	<i>-o^(b)-</i>	other
<i>-k-</i>	cytokine	<i>-u^(c)-</i>	untargeted
<i>-m-</i>	membrane protein		
<i>-n-</i>	enzyme		
<i>-p-</i>	apoptosis		
<i>-r-</i>	receptor		
<i>-t-</i>	T-cell receptor		
<i>-v^(a)-</i>	multiple actions/proteins		
<i>-x-</i>	toxin		

^(a) *-v-* will be used when a multifunctional fusion protein has multiple and not related actions;

^(b) *-o-* will be used when some other targeting mechanism (i.e. not antibody, receptor or antigen) is used in a bifunctional fusion protein or in a multifunctional fusion protein with multiple unrelated targeting;

^(c) *-u-* will be used when a fusion protein has multiple actions and no targeting;

2.4. General policy for pegylated substances [22]

Two different approaches have been used for pegylated substances (see ANNEX 3):

- a single-word scheme with the prefix *peg-* (e.g. *peginterferon alfa-2a (84)*, *pegaldesleukin (74)*);
- a two-word scheme with the first word representing the biological substance and the second word *pegol*. To avoid over-long INN, the two-word scheme has been preferred for names with long stems (e.g. *alacizumab pegol (98)*, *calaspargase pegol (105)*).

In a few cases, a fantasy prefix has been added to an existing *peg-* INN to accommodate a new INN request for a similar substance. This has the effect of changing the *peg-* from a

prefix to an infix (e.g. *peginterferon alfa-2b* (84) and *cepeginterferon alfa-2b* (105); *pegfilgrastim* (86) and *empegfilgrastim* (107)).

Note: There is no implied difference relating to the use of the different schemes.

2.5. General policy for substances for gene therapy [2]

In 2005, a two-word nomenclature scheme for substances for gene therapy was formally adopted by the members of the INN Expert Group designated to deal with the selection of nonproprietary names. The 2016 updated scheme for substances for gene therapy using vectors based on recombinant nucleic acid sequences (DNA vectors, e.g. plasmid DNA, naked or complexed), genetically modified micro-organisms (bacterial vectors) or viruses (replication defective, replication competent or replication conditional viral vectors) is shown in Table 2. See section 2.7: General policy for substances for cell-based gene therapy for the nomenclature scheme for substances for cell-based gene therapy, which is based on administration of genetically modified cells, for which typically a viral vector is used *ex-vivo* or *in-vitro* for manufacturing of those cells prior to administration.

Table 2: Two-word scheme for substances for gene therapy (plasmid-, viral vector- and bacterial-based).

	Prefix	Infix	Suffix
word 1 (gene component)	random to contribute to euphonious and distinctive name	to identify the gene using, when available, existing infixes for biological products, e.g.: <i>-cima-</i> cytosine deaminase <i>-ermin-</i> growth factor <i>-kin-</i> interleukin <i>-lim-</i> immunomodulator <i>-lip-</i> human lipoprotein lipase <i>-mul-</i> multiple gene <i>-stim-</i> colony stimulating factor <i>-tima-</i> thymidine kinase <i>-tusu-</i> tumour suppression	-(a vowel) <i>gene</i> e.g. -(o) <i>gene</i>
word 2 (vector component)	random to contribute to euphonious and distinctive name	to identify the viral vector type, e.g.: <i>-adeno-</i> adenovirus <i>-cana-</i> canarypox virus <i>-foli-</i> fowlpox virus <i>-erpa-</i> herpes virus <i>-lenti-</i> lentivirus <i>-morbilli-</i> Paramyxoviridae morbillivirus <i>-parvo-</i> adeno-associated virus (Parvoviridae dependovirus) <i>-retro-</i> other retrovirus <i>-vaci-</i> vaccinia virus	- <i>vec</i> (non-replicating viral vector) - <i>repvec</i> (replicating viral vector)
		to identify the bacterial vector type, e.g.: <i>-lis-</i> <i>Listeria monocytogenes</i>	- <i>bac</i> (bacteria vector)
		(none)	- <i>plasmid</i> (plasmid vector)

In the case of substances for gene therapy based on non-plasmid DNA, there is at present no need for a second word in the name.

2.6. General policy for substances for cell therapy

During the 63rd INN Consultation in 2016, an INN-USAN-harmonized nomenclature scheme for substances for cell therapy was formally approved by the members of the INN Expert Group designated to deal with the selection of international nonproprietary names³.

Substances for cell therapy are given a one-word name. Table 3 shows the nomenclature scheme to name all non-genetically modified substances for cell therapy, with the exception of minimally manipulated hematopoietic elements and combinations of substances, which are not named. For genetically modified substances for cell therapy, please see section 2.7.

Table 3: Nomenclature scheme for non-genetically modified substances for cell therapy.

Prefix	Infix: cell type	Suffix
random to contribute to euphonious and distinctive name.	to identify the primary cell type ^(c) using, when available, existing infixes for cell types ^(d)	- <i>cel</i> (cell)

^(a) There may be more than one manipulation infix in the same INN, but should be avoided if possible to avoid overly long names.

^(b) In the case of manipulation such as cell expansion and cell activation (with cytokines/drug, etc.), there is no need for an infix; this kind of manipulation will be specified in the description.

^(c) Residual cells not expected to contribute to the intended function, are not named.

^(d) - <i>adstro</i> -	adipose stromal cells	- <i>mestro</i> -	mesenchymal stromal cells (MSC)
- <i>co(n)</i> -	chondrocytes	- <i>mio(b)</i> -	myoblasts
- <i>ubi</i> -	umbilical cord cells	- <i>ova</i> -	ovary cells
- <i>defitem</i> -	differentiated stem cells (not fitting into any existing category)	- <i>pla(c)</i> -	placenta cells
- <i>den</i> -	dendritic cells	- <i>ren</i> -	renal tubular cells
- <i>end(o)</i> -	endothelial cells	- <i>ret</i> -	retinal epithelial cells
- <i>ep(a)</i> -	hepatocytes	- <i>tem</i> -	stem cells
- <i>fi(b)</i> -	fibroblasts	- <i>tesi</i> -	testis cells
- <i>isle</i> -	islet cells	- <i>tu</i> -	tumor cells
- <i>ker(a)</i> -	keratinocytes	- <i>ur</i> -	urothelial cells
- <i>leu</i> -	lymphocytes/monocytes/APC (white cells) ^(e)		

^(e) The cell type infix -*leu*- is used to describe hematologic cell preparations that do not fit in a particular or specific cell type category. Such cell preparations may be comprised of a mixture of the

³ INN selected before the adoption of the present nomenclature scheme may have followed different rules.

various blood cell elements, a subset of blood elements such as T-, B- or NK-cells, or antigen-presenting cells (APCs) that do not fit in the definition of dendritic cells.

Note: Information concerning manipulation and/or modification, and the type of the cell-based therapy (i.e. allogeneic, autologous and xenogeneic), will be specified in the description of the product.

2.7. General policy for substances for cell-based gene therapy

During the 63rd INN Consultation in 2016, an INN-USAN-harmonized nomenclature scheme for substances for cell-based gene therapy was formally approved by the members of the INN Expert Group designated to deal with the selection of international nonproprietary names⁴.

A two-word name is given to substances for cell-based gene therapy, in which the first word refers to the gene component and the second word refers to the cell component. The first word is named in the same way as the first word for substances for gene therapy (see Table 2).

During the 67th INN Consultation in 2018, an INN-FDA harmonised scheme for *autologous* substances for cell-based gene therapy was formally approved by the members of the INN Expert Group designated to deal with the selection of international non-proprietary names⁴.

Table 4 shows the nomenclature scheme to name all genetically modified substances for cell-based gene therapy, with the exception of minimally manipulated hematopoietic elements and combinations of substances, which are not named.

Table 4: Nomenclature scheme for genetically modified substances for cell-based therapy.

	Prefix	Infix	Suffix
word 1 (gene component)	random to contribute to euphonious and distinctive name.	to identify the gene using, when available, existing infixes for biological products or using similar infix as for the protein for which the gene codes, e.g.: <i>-cabta-</i> cell expressed antibody and T cell activation <i>-cima-</i> cytosine deaminase <i>-ermin-</i> growth factor <i>-kin-</i> interleukin <i>-lim-</i> immunomodulator <i>-lip-</i> human lipoprotein lipase <i>-mul-</i> multiple gene <i>-stim-</i> colony stimulating factor <i>-tima-</i> thymidine kinase <i>-tusu-</i> tumour suppression	-(a vowel) <i>gene</i> e.g. -(o) <i>gene</i>
word 2 (cell component)	autologous: <i>auto-</i> allogenic: <i>random</i>	to identify the primary cell type ^(c) using, when available, existing infixes for cell types ^(d)	<i>-cel</i> (cell)

(a) (b) (c) (d) See the footnotes (a), (b), (c) and (d) on the preceding page.

⁴ INN selected before the adoption of the present nomenclature scheme may have followed different rules.

Note: Extensive information concerning manipulation and/or modification, and the type of the cell-based therapy (i.e. allogeneic, autologous and xenogeneic), is provided in the description of the substance.

2.8. General policy for substances for virus-based therapy

Substances for virus-based therapy are those for which the virus itself is acting as a therapeutic agent. This is distinct from virus-based gene therapy in which the virus is acting as a carrier of a therapeutic gene. In some cases, the virus may be genetically modified to enhance the therapeutic effect of the virus. To date, the only virus-based therapies that have been named are oncolytic viruses whereby the virus is used to target and destroy cancer cells.

In the event that a virus-based therapy such as an oncolytic virus is genetically modified to express a therapeutic gene, the virus-based gene therapy nomenclature scheme should be used.

Table 5 shows the nomenclature scheme for substances for virus-based therapy⁵.

Table 5: Nomenclature scheme for substances for virus-based therapy.

Prefix	Infix 1: virus type	Infix 2:	Suffix
random to contribute to euphonious and distinctive name.	<i>-adeno-</i> adenovirus <i>-cana-</i> canarypox virus <i>-foli-</i> fowlpox virus <i>-erpa-</i> herpes virus <i>-lenti-</i> lentivirus <i>-morbilli-</i> Paramyxoviridae morbillivirus <i>-parvo-</i> adeno-associated virus (Parvoviridae dependovirus) <i>-retro-</i> other retrovirus <i>-vaci-</i> vaccinia virus	<i>-tu-</i> for tumoricidal	<i>-rev</i> (therapeutic virus)

2.9. General policy for monoclonal antibodies [1, 3, 11, 23]⁶

- The stem **-mab** is used for all substances that contain an immunoglobulin variable domain that binds to a defined target, and that are composed of only one pharmacologically active component, unless the other(s) pharmacologically active component(s) is(are) a mAb. The stem is preceded by an infix that indicates the target class (molecule, cell and organ) (Table 6).

⁵ INN selected before the adoption of the present nomenclature scheme may have followed different rules.

⁶ It contains the revised naming scheme for monoclonal antibodies; the previous naming scheme for monoclonal antibodies is given in ANNEX 5.

- Deletion of the ‘species infix’ was formally approved during the 64th INN Consultation by the members of the INN Expert Group designated to deal with the selection of international nonproprietary names.
- Full information including the development of the mAb on which the immunoglobulin sequence of the mAb is based, is included in the definition of the INN for mAbs.

Table 6: Nomenclature scheme for monoclonal antibodies (mAb).

Prefix:	Infix: target class	Stem:
random	<i>-ami-</i> serum amyloid protein (SAP)/amyloidosis (<i>pre-substem</i>) <i>-ba-</i> bacterial <i>-ci-</i> cardiovascular <i>-de-</i> metabolic or endocrine pathways <i>-fung-</i> fungal <i>-gros-</i> skeletal muscle mass related growth factors and receptors (<i>pre-substem</i>) <i>-ki-</i> interleukin <i>-li-</i> immunomodulating <i>-ne-</i> neural <i>-os-</i> bone <i>-ta-</i> tumour <i>-toxa-</i> toxin <i>-vet-</i> veterinary use (<i>sub-stem</i>) <i>-vi-</i> viral	<i>-mab</i>

Second word

If the monoclonal antibody is conjugated to another protein or to a chemical (e.g. chelator), identification of the conjugate is accomplished by use of a separate, second word or acceptable chemical designation. For mAbs conjugated to a toxin, the suffix *-tox* is used in the second word.

If the monoclonal antibody is radiolabelled, the radioisotope is listed first in the INN, e.g. *technetium (^{99m}Tc) nofetumomab merpentan (81)*.

Pegylation

For pegylated monoclonal antibodies see item 2.4: General policy for pegylated substances.

Glycosylation

For glycosylated monoclonal antibodies see item 2.2: General policy for glycosylated substances.

2.10. General policy for blood products [4]

- INN are not assigned to natural human blood products.
- Many natural blood products have well-established names; the recombinant version should have a distinctive name reflecting as much as possible the established name used in the field.

- It is essential to add "activated" to the name of the blood product when this is presented for therapeutic use in its activated form.

2.11. General policy for immunoglobulins fractionated from plasma [9, 10]

- INN are not assigned to immunoglobulins fractionated from plasma.
- The "systematic" or descriptive name is essential since the prescriber must know all the information conveyed by it and there is no benefit in assigning an INN from which it will not be readily apparent.

2.12. General policy for skin substitutes [4]

INN are not assigned to skin substitutes. These substances are made of cells within a matrix that are considered to be engineered tissue and thus fall outside the scope of the INN system.

2.13. General policy for transgenic substances [4]

- If an INN already exists, the same name should be used for the transgenic product, qualified in some way to identify that this product is transgenic.
- A similar system to that used for glycosylated recombinant products is suggested to differentiate new or additional sources of the same substance, and the source of the substance should be included in the definition of the INN (e.g. *antithrombin alfa (93)* (Rec. Glycoprotein (432aa) from transgenic goats)).

2.14. General policy for vaccines [4-7]

- Vaccines are traditionally considered to be medicinal substances used to stimulate an individual's immune system into providing protection against a particular infectious disease. Traditional vaccines consist of whole killed pathogens, live attenuated pathogens, subunits (antigens) derived from pathogens, or inactivated pathogenic toxins.
- With the advent of recombinant DNA technology, novel approaches for the development of vaccines against infectious diseases were developed including recombinant DNA expressed protein antigens, recombinant DNA derived virus-like particles, recombinant live vectors expressing heterologous antigens, and DNA/RNA vaccines.

- Another approach in vaccine technology is the development of peptide vaccines⁷ (epitopes involved in immune response formation). Since these peptides are chemically well-defined, they fall within the INN naming system.
- In addition to vaccines against infectious diseases, the term vaccine is also being applied to other medicinal substances such as ‘cancer vaccines’ typically containing a tumour antigen with the intention of stimulating the immune system to attack and destroy the tumour. Many so-called cancer vaccines consist of synthetic peptides that comprise all or part of a tumour antigen.
- At present, vaccines are not included within the INN system, with names being assigned through recommendations of the Expert Committee on Biological Standardization and through pharmacopoeial monographs.
- During the INN Consultation in 1993, it was agreed that the prerequisite for an INN application for a recombinant vaccine⁸ would be fulfilled if the manufacturer was able to provide all information outlined in the guidelines entitled Definition of INNs for Substances Prepared by Biotechnology (WHO/Pharm S/Nom 1348 [12]).

⁷ The definition of peptide vaccines is given in item 3.37.

⁸ The definition of recombinant vaccines is given in item 3.37.

3. SUMMARY OF INN ASSIGNED TO BIOLOGICAL AND BIOTECHNOLOGICAL SUBSTANCES [1, 3, 7, 8, 13-21]

3.1. Antimicrobial, bactericidal permeability increasing polypeptides

The pre-stem for antimicrobial, bactericidal permeability increasing polypeptides is **-ganan**.
iseganan (85)⁹, *omiganan* (89), *pexiganan* (78).

3.2. Antisense oligonucleotides¹⁰

The common stem for antisense oligonucleotides is **-rsen**:

aganirsen (103), *alicaforsen* (118), *anivamersen* (105), *apatorsen* (110), *aprinocarsen* (97), *atesidorsen* (116), *beclanorsen* (101), *cenersen* (97), *cobomarsen* (117), *custirsen* (99), *danvatirsen* (117), *eluforsen* (119), *gataparsen* (103), *inotersen* (115), *lademirsen* (120), *mipomersen* (100), *mongersen* (111), *oblimersen* (97), *prexigebersen* (114), *remlarsen* (117), *tofersen* (120), *trabedersen* (98), *volanesorsen* (113).

The suffix **-nersen** designates *neurological disorders* antisense oligonucleotides:

nusinersen (112),

The suffix **-dirsen** designates *muscular dystrophies* antisense oligonucleotides:

golodirsen (115), *renadirsen* (120),

Exceptions: (belong to this group, but the suffix **-dirsen** has not been used):

baliforsen (116), *casimersen* (115), *dematirsen* (116), *drisapersen* (106), *eteplirsen* (103), *rimigorsen* (116), *varodarsen* (116), *viltolarsen* (118).

The substem **-virsen** designates *antiviral* antisense oligonucleotides:

afovirsen (97), *amlivirsen* (119), *fomivirsen* (97), *miravirsen* (101), *radavirsen* (106), *temavirsen* (117), *trecovirsen* (97).

3.3. Antithrombins

antithrombin III (60), *antithrombin alfa* (93) (Rec. Glycoprotein, 432aa, from transgenic goats), *antithrombin gamma* (116).

⁹ The numbers in parentheses indicate the Proposed list number.

¹⁰ For small interfering RNA see item 3.32 and for various see item 3.38.

3.4. Aptamers, classical and mirror ones

The common stem for aptamers is **-apt-**:

avacincaptad pegol (113), egaptivon pegol (111), emapticap pegol (108), lexaptepid pegol (108), olaptosed pegol (109), pegaptanib (88)

Exceptions: (belong to this group, but the preferred stem has not been used):

pegnivacogin (106)

3.5. Blood coagulation cascade inhibitors

The common stem for blood coagulation cascade inhibitors is **-cogin**.

drotrecogin alfa (activated) (86), pegnivacogin (106), taneptacogin alfa (90), tifacogin (78).

3.6. Blood coagulation factors

The common stem for blood coagulation factors is **-cog**.

The substems **-eptacog**, **-octocog**, **-nonacog/-trenonacog** and **-tridecacog** have been selected to date for recombinant blood coagulation factors.

- A prefix will be necessary if the amino acid sequence does not match that of the naturally occurring material.
- In accordance with the general policy, *alfa*, *beta*, etc, will be added for the glycoproteins (see item 2.2: General policy for glycosylated substances).
- When the additional statement "*activated*" is needed, e.g. for the blood coagulation factor VIIa, it should be spelt out in full and added in parentheses after the name.

-eptacog (factor VII):

eptacog alfa (activated) (77), eptacog alfa pegol (activated) (101), eptacog beta (activated) (112), marzeptacog alfa (activated) (113), oreptacog alfa (activated) (109), vatreptacog alfa (activated) (98)

-octocog (factor VIII):

beroctocog alfa (112), damoctocog alfa pegol (109), efmoroctocog alfa (111), lonoctocog alfa (111), moroectocog alfa (72), octocog alfa (73), rurioctocog alfa pegol (111), simoectocog alfa (104), susoectocog alfa (112), turoctocog alfa (108), turoctocog alfa pegol (108)

-nonacog (factor IX with Ala at the position 148 (Ala-alloform)):

albutrepenonacog alfa (109), dalcinonacog alfa (118), nonacog alfa (77), nonacog beta pegol (104), nonacog gamma (108)

-trenonacog (factor IX with Thr at the position 148 (Thr-alloform))

eftrenonacog alfa (109), trenonacog alfa (107)

-tridecacog (factor XIII):

catridecacog (99)

-vonico (recombinant von Willebrand factor (vWF)):

vonico alfa (120)

3.7. Substances for gene therapy

For the general policy for substances for gene therapy see item 2.5.

Viral vectors:

adlinacogene civaparvovec (120), aglatimagene besadenovec (113), alferminogene tadenovec (95), alipogene tiparvovec (99), betibeglogene darolentivec (116), cadalimogene ixalentivec (120), contusogene ladenovec (97), delolimogene mupadenorepvec (118), devafidugene civaparvovec (120), eladocogene exuparvovec (119), elivaldogene tavalentivec (115), eretidigene velentivec (115), etranacogene dezaparvovec (120), fidanacogene elaparvovec (118), golnerminogene pradenovec (101), inlezipigene civaparvovec (120), lanacogene vosiparvovec (117), lenadogene nolparvovec (114), mesmulogene ancovacivec (114), nadofarogene firadenovec (117), ofranergene obadenovec (115), olenasuflogene relduparvovec (119), onasemnogene abeparvovec (117), pexastimogene devacirepvec (108), ranuzifigene civaparvovec (120), rebisufligene etisparvovec (118), resamirigene bilparvovec (120), riferminogene pecaplasmid (100), rilimogene galvacirepvec (107), rilimogene glafolivec (113), rovoctocogene durparvovec (120), sitimagene ceradenovec (97), taberminogene vadenovec (100), talimogene laherparepvec (104), tefidsogene civaparvovec (120), timrepigene emparvovec (117), tipapkinogene sovacivec (102), valoctocogene roxaparvovec (116), vocimagene amiretrorepvec (107), volrubigene ralaparvovec (120), voretigene neparvovec (115),

Bacterial vectors:

axalimogene filolisbac (112), miralimogene ensolisbac (117), opolimogene capmilisbac (117), pemlimogene merolisbac (117)

Plasmids:

amolimogene bepiplasmid (98), beperminogene perplasmid (95), bizalimogene ralaplasmid (118), donaperminogene seltoplasmid (116), inodiftagene vixteplasmid (120), mavilimogene ralaplasmid (118), tavokinogene telseplasmid (118), tirvalimogene teraplasmid (117), velimogene aliplasmid (97)

3.8. Substances for cell therapy

For the General policy for substances for cell therapy see item 2.6.

adimlecleucel (117), audencel (115), avoplacel (119), baltaleucel (116), cenplacel (115), darvadstrocel (117), dilanubicel (119), eltrapuldencel (115), emiplacel (118), ilixadencel (116), lenzumestrocel (119), lifileucel (118), mocemestrocel (120), palucorcel (115), spanlecortemlocel (115), tabelecleucel (117), vandefitemcel (115)

3.9. Substances for cell-based gene therapy

For the General policy for substances for cell-based gene therapy see item 2.7.

axicabtagene ciloleucel (117), evagenretcel (116), idecabtagene vicleucel (119), lisocabtagene maraleucel (119), nalotimagene carmaleucel (118), prademagene zamikeracel (119), rivogenlecleucel (117), tisagenlecleucel (117), tonogenconcel (115), vadacabtagene leraleucel (117)

3.10. Substances for virus-based therapy

For the General policy for substances for virus-based therapy see item 2.8.

canerpaturev (117), enadenotucirev (111), tasadenoturev (117), teserpaturev (119)

3.11. Colony stimulating factors (CSF)

The common stem for colony stimulating factors (CSF) is **-stim**.

*ancestim (79) (cell growth factor),
garnocestim (86) (immunomodulator),
pegacaristim (80) (megakaryocyte growth and development factor (MGDF))¹¹,
romiplostim (97) (platelet stimulating factor (through thrombopoietin receptor(Mpl)))¹²*

-distim for combination of two different types of CSF:

leridistim (80), milodistim (75)

-gramostim for granulocyte macrophage (GM)-CSF type substances:

ecogramostim (62), molgramostim (64), regramostim (65), sargramostim (66)

-grastim for granulocyte (G)-CSF type substances:

*balugrastim (107), eflapegrastim (112), eflenograstim alfa (117), empegfilgrastim (107),
filgrastim (64), lenograstim (64), lipegfilgrastim (107), mecapegfilgrastim (113),*

¹¹ Also known as thrombopoietin.

¹² A thrombopoietin mimetic.

nartograstim (66), pegbovigrastim (109), pegfilgrastim (86), pegnartograstim (80), pegteograstim (109)

-mostim for macrophage (M)-CSF type substances:

cilmostim (71), lanimostim (91), mirimostim (65)

-plestim for interleukin-3 analogues and derivatives:

daniplestim (76), muplestim (74).

3.12. Enzymes

The common stem for enzymes, in general, is **-ase**.

Enzymes are classified according to an enzyme classification (E.C.) number, i.e, the reaction they catalyse¹³.

Substems are referring, in general, to the activity of the substances.

- EC 1.7.3.3 Factor independent urate hydroxylase (uricase):

-icase for uricase (*suffix*)

pegadricase (105), pegloticase (98), rasburicase (82)

- EC 1.15.1.1 Superoxide dismutase:

-dismase for dismutase (enzymes with superoxide dismutase activity)

ledismase (70), sudismase (58)

Exceptions: (belong to this group, but the preferred stem has not been used)

orgotein (31), pegorgotein (72)

- EC 2.4.2 Pentosyltransferases:

praconase (118)

- **-lipase** for lipase:

EC 3.1.1.3 Triacylglycerol lipase

burlulipase (107), rizolipase (22)

EC 3.1.1.13 Sterol esterase

bucelipase alfa (95), sebelipase alfa (107)

- EC 3.1.1.71 Acetylalkylglycerol acetylhydrolase

epafipase (85)

- EC 3.1.3.1 Alkaline phosphatase

asfotase alfa (104)

¹³ For enzyme classification and nomenclature see:

<http://www.chem.qmul.ac.uk/iubmb/enzyme> ; <http://www.brenda-enzymes.org>

- EC 3.1.4.12 Sphingomyelin phosphodiesterase
olipudase alfa (111)
- **-sulfase** for sulfatases (*suffix*):
 - EC 3.1.6.4 *N*-Acetylgalactosamine-6-sulfatase
elosulfase alfa (108)
 - EC 3.1.6.12 *N*-Acetylgalactosamine-4-sulfatase
galsulfase (92)
 - EC 3.1.6.13 Iduronate-2-sulfatase
idursulfase (90), idursulfase beta (106)
- EC 3.1.21.1 Deoxyribonuclease I:
-dornase for deoxyribonuclease (*suffix*)
alidornase alfa (115), dornase alfa (70), streptodornase (6)
- EC 3.1.27.5 Pancreatic ribonuclease
ranpirnase (81)
- EC 3.2.1.17 Lysozyme (muramidase)
exebacase (117), tonabacase (115)
- EC 3.2.1.20 α -Glucosidase
alglucosidase alfa (117), avalglucosidase alfa (117), reveglucosidase alfa (111)
- EC 3.2.1.22 α -Galactosidase
agalsidase alfa (84), agalsidase beta (84), pegunigalsidase alfa (115)
- EC 3.2.1.23 β -Galactosidase
tilactase (50)
- EC 3.2.1.24 α -Mannosidase
velmanase alfa (113)
- EC 3.2.1.26 β -fructofuranosidase (β -fructosidase, invertase, saccharase)
sacrosidase (112)
- EC 3.2.1.31 β -glucuronidase
vestronidase alfa (115)
- EC 3.2.1.35 Hyaluronoglucosaminidase
bovhyaluronidase azoximer (112), hyalosidase (50), hyaluronidase (1), pegvorhyaluronidase alfa (115), vorhyaluronidase alfa (111)

- EC 3.2.1.45 Glucosylceramidase:
-glucerase for glucosylceramidase (*suffix*)
alglucerase (68), imiglucerase (72), taliglucerase alfa (101), velaglucerase alfa (98)
- EC 3.2.1.50 α -N-Acetylglucosaminidase
lesinidase alfa (116), tralesenidase alfa (117)
- EC 3.2.1.76 L-iduronidase
laronidase (86)
- EC 3.4.14.9 Tripeptidyl-peptidase 1
cerliponase alfa (111)
- EC 3.4.17.11 Glutamate carboxypeptidase
glucarpidase (92)
- EC 3.4.21. Serine endopeptidases
eufausease (84), senrebotase (107), sfericase (40)
- EC 3.4.21.35 Tissue kallikrein
kallidinogenase (22)
- EC 3.4.21.36 Pancreatic elastase
vonapanitase (111)
- EC 3.4.21.63 Oryzin
promelase (47), serrapeptase (31)
- EC 3.4.21.68 t-Plasminogen activator:
-teplase for tissue-type plasminogen activators
alteplase (73), desmoteplase (80), dutiplase (62), lanoteplase (76), monteplase (72), nateplase (73), pamiteplase (78), reteplase (69), silteplase (65), tenecteplase (79)

 Exception: streptokinase (activity related to this group), modified stem **-streplase**
anistreplase (59)
- EC 3.4.21.73 u-Plasminogen activator:
-uplase for urokinase(urinary)-type plasminogen activators
nasaruplase (76), nasaruplase beta (86), saruplase (76)

 Exceptions (belong to this group, but the preferred stem has not been used):
urokinase (48), urokinase alfa (77)
- EC 3.4.21.68 / 3.4.21.73:
-diplase for two plasminogen activators combined with another enzyme
amediplase (79)

- EC 3.4.22.10 Streptopain (Streptococcal cysteine proteinase, Streptococcus peptidase A):
imlifidase (117)
- EC 3.4.24.72 Fibrolase
alfimeprase (85), brinase (22), ocrase (28)
- EC 3.4.24.87 ADAMTS13 endopeptidase
apadamase alfa (118)
- EC 3.5.1.1 L-Asparaginase
calaspargase pegol (105), crisantaspase (111), pegaspargase (64), pegcrisantaspase (111)
- EC 3.5.2.6 β -Lactamase
penicillinase (111), ribaxamase (116)
- EC 3.5.3.1 Arginine amidinase
pegzilarginase (117)
- EC 3.5.3.6 Arginine deiminase
pegargininase (111)
- EC 3.5.4.4 Adenosine deaminase
elapegademase (116), pegademase (63)
- **-liase** for lyase (decarboxylase) (*suffix*):
 - EC 4.1.1.2 Oxalate decarboxylase
reloxaliase (117)
 - EC 4.2.2.20 Chondroitin-sulfate-ABC endolyase
condoliase (106)
 - EC 4.3.1.24 Phenylalanine ammonia-lyase
pegvaliase (111)
- Exceptions, without **-ase** stem:
 - chymotrypsin (10) (EC 3.4.21.1), thrombin (60) (E C.3.4.21.5), thrombin alfa (97)(EC. 3.4.21.5), fibrinolysin (human) (10) (3.4.21.7), ocriplasmin (101) (3.4.21.7), troplasminogen alfa (99), ancrod (23) (EC 3.4.21.74), batroxobin (29) (EC 3.4.21.74), chymopapain (26) (E C 3.4.22.6), bromelains (18) (EC 3.4.22.32/33), sutilains (18)(EC 3.4.21.62)*
- Co-enzymes:
 - cobamamide (15)(!), cocarboxylase (1), mecobalamin (26) (!), streptokinase (6), ubidecarenone (48)*

3.13. Erythropoietin type blood factors

The common stem for erythropoietin type blood factors is **-poetin**.

In the case of erythropoietins, it was decided to select *epoetin* together with a Greek letter to differentiate between substances of the same amino acid sequence as human erythropoietin which vary in the glycosylation pattern (see item 2.2: General policy for glycosylated substances).

Substances with different amino acid sequences will be named using the *-poetin* stem and unique random prefixes.

darbepoetin alfa (85), efepoetin alfa (117), epoetin alfa (66), epoetin beta (62), epoetin gamma (67), epoetin delta (85), epoetin epsilon (72), epoetin zeta (95), epoetin theta (95), epoetin kappa (97), epoetin omega (73), pegdarbepoetin beta (117)

3.14. Fusion proteins with more than one pharmacologically active component

The common stem for fusion proteins with more than one pharmacologically active component is **-fusp**.

bifikafusp alfa (118), bintrafusp alfa (119), clervonafusp alfa (120), lorukafusp alfa (120), onfekafusp alfa (118), pabinafusp alfa (120), rozibafusp alfa (120), tagraxofusp (118), tebentafusp (118), valanafusp alfa (118),

3.15. Gonadotropin-releasing hormone (GnRH) inhibiting peptides

The common stem for gonadotropin-releasing hormone (GnRH) inhibiting peptides is **-relix**.

abarelix (78), cetrorelix (66), degarelix (86), detirelix (56), ganirelix (65), iturelix (79), ozarelix (94), prazarelix (81), ramorelix (69), teverelix (78).

3.16. Growth factors and tumour necrosis factors (TNF)

The common stem for growth factors and tumour necrosis factors (TNF) is **-ermin**.

Substems allow distinction between the various types of growth factors.

-bermin for vascular endothelial growth factors:

telbermin (85)

-dermin for epidermal growth factors:

murodermin (63), nepidermin (97)

-fermin for fibroblast growth factors:

aldafermin (120), ersofermin (66), palifermin (88), pegbelfermin (120), repifermin (82), sprifermin (105), trafermin (74), velafermin (94)

-filermin for leukaemia-inhibiting factors:

emfilermin (82)

-nermin for tumour necrosis factors:

ardenermin (88), dulanermin (99), efgivanermin (120), efaprienermin alfa (120), eftozanermin alfa (119), plusonermin (73), sonermin (68), tasonermin (78), tengonermin (118)

-plermin for platelet-derived growth factors:

becaplermin (74)

-sermin for insulin-like growth factors:

mecasermin (66), mecasermin rinfabate (92)

-termin for transforming growth factors:

cetermin (74), liatermin (81)

-otermin for bone morphogenetic proteins:

avotermin (77), dibotermin alfa (89), eptotermin alfa (92), nebotermin (109), radotermin (92)

Others:

*cenegermin (115) human beta-nerve growth factor (beta-NGF)
cimaglermin alfa (110) (recombinant DNA derived glial growth factor 2 (GGF2))
dapiclermin (93) (modified ciliary neurotrophic factor (CNTF)).*

3.17. Growth hormone (GH) derivatives

The common stem for growth hormone (GH) derivatives is **som-**.

Human growth hormone derivatives:

albusomatropin (114), efpegsomatropin (115), eftansomatropin alfa (118), lonapegsomatropin (118), somapacitan (112), somatrem (54), somatrogon (115), somatropin (74), somatropin pegol (103), somavaratan (112)

For substances other than human, suffixes are added to indicate the species specificity of the structure.

-bove for bovine-type substances:

somagrebove (63), somavubove (63), sometribove (74), somidobove (58)

-por for porcine-type substances:

somalapor (62), *somenopor* (62), *somfasepor* (66), *sometripor* (75)

-salm for salmon-type substances:

somatosalm (69)

Others (growth hormone related peptides):

somatorelin (57) (pituitary hormone-release stimulating peptides, see item 3.30)

somatostatin (46) (growth hormone release inhibitor).

3.18. Growth hormone (GH) antagonists

pegvisomant (82)

3.19. Heparin derivatives including low molecular weight heparins

The common stem for heparin derivatives including low molecular weight heparins is **-parin**.

ardeparin sodium (68), *adomiparin sodium* (104), *bemiparin sodium* (75), *certoparin sodium* (70), *dalteparin sodium* (77), *deligoparin sodium* (89), *enoxaparin sodium* (77), *heparin sodium* (54), *livaraparin calcium* (86), *minolteparin sodium* (74), *nadroparin calcium* (78), *parnaparin sodium* (77), *reviparin sodium* (78), *semuloparin sodium* (99), *sevuparin sodium* (106), *tafoxiparin sodium* (102), *tinzaparin sodium* (77).

3.20. Hirudin derivatives

The common stem for hirudin derivatives is **-irudin**.

bivalirudin (72), *desirudin* (76), *lepirudin* (76), *pegmusirudin* (77).

3.21. Immunomodulators, both stimulant/suppressive and stimulant

The common stem for immunomodulators, both stimulant/suppressive and stimulant, is **-imod**.

-tol- (Toll-like receptors (TLR) agonists):

agatolimod (98) (TLR9 agonist with 24-mer modified oligodeoxynucleotides (ODN))

cobitolimod (113) (sodium salt of DNA-based immunomodulatory sequence (DIMS) that binds to toll-like receptor (TLR) 9)

entolimod (108) (natural activator of toll-like receptor 5 (TLR5))

lefitolimod (113) (DNA based immunomodulator agent)

rintatolimod (102) (TLR3 agonist)

tilsotolimod (117) (TLR9 agonist)

Exceptions: (belong to this group, but the preferred substem has not been used):

litenimod (96) (TLR9 agonist, 26-mer modified oligodeoxynucleotides (ODN))

Others:

bevifimod (119) (staphylococcal protein A (SpA), purified from *Staphylococcus aureus* strain A676 culture medium)

blisibimod (107) (B-cell activating factor (BAFF)-binding peptide fragment/human IgG1 Fc fusion protein)

cupabimod (115) (DNA based immunomodulator agent)

efgartigimod alfa (116) (mutated human immunoglobulin G1 Fc fragment, covalent dimer)

efizonerimod alfa (117) (modified human immunoglobulin G4 Fc fragment fused to tumor necrosis factor receptor-associated factor TRAF2 (human C-C domain fragment) and to the CD252 antigen (human extracellular domain fragment), hexamer)

eftilagimod alfa (116) (human lymphocyte activation gene 3 protein extracellular domains fused to human immunoglobulin G1 Fc fragment through a linker peptide, covalent dimer)

reltecimod (115) (T-cell-specific surface glycoprotein CD28 (8-15)-peptide)

3.22. Insulins

Up to now, insulin derivatives have been named using a two-word approach. The substances named represent a structure with an additional amino acid, such as *insulin argine (58)*, or represent modifications of the amino acid sequence, i.e. *insulin aspart (76)*.

biphasic insulin injection (16), *compound insulin zinc suspension (06)*, *dalanated insulin (104)*, *globin zinc insulin injection (06)*, *insulin argine (58)*, *insulin aspart (76)*, *insulin defalan (37)*, *insulin degludec (101)*, *insulin detemir (80)*, *insulin glargine (76)*, *insulin glulisine (84)*, *insulin human (48)*, *insulin lispro (72)*, *insulin peglispro (107)*, *insulin tregopil (103)*, *insulin zinc suspension (amorphous) (04)*, *insulin zinc suspension (crystalline) (04)*, *isophane insulin (04)*, *neutral insulin injection (15)*, *protamine zinc insulin injection (06)*

argine: B30-yl-L-arginyl-L-arginine

aspart: [B28-L-aspartic acid]

dalanated: des-B30-alanine

defalan: des-B1-phenylalanine

degludec: $N^{6.B29}$ -[N-(15-carboxypentadecanoyl)-L- γ -glutamyl]-des-30B-L-threonine

detemir: $N^{6.B29}$ -tetradecanoyl-des-B30-L-threonine

glargine: [A21-glycine], B30-yl-L-arginyl-L-arginine

glulisine: [B3-lysine, B29-glutamic acid]

lispro: [B28-L-lysine, B29-L-proline]

tregopil: N^{6,B29}-(4,7,10,13-tetraoxatetradecanoyl).

3.23. Interferons

Interferon was published as an INN in 1962 with a general definition based on the origin and activity, e.g. "a protein formed by the interaction of animal cells with viruses capable of conferring on animal cells resistance to virus infection".

The name was revised in the 1980s when human interferon and its variations *alfa*, *beta* and *gamma* were produced by recombinant biotechnology. The INN Expert Group would have preferred to replace the old INN interferon by alfaferon, betaferon and gammaferon; however, this approach could not be adopted as these names had already been registered as trade marks. The system adopted was thus to take interferon alfa, interferon beta and interferon gamma, and to provide, when necessary, for further distinction by additional numbers. Thus Arabic numbers are used to distinguish subspecies which differ significantly in primary amino acid sequence, but are still considered to belong to one of the primary groups e.g. interferon alfa-1, interferon alfa-2. Small (lower case) letters are used to subdivide such groups further on the basis of less significant differences like one, two or three amino acid differences or post translational modifications, including glycosylation e.g. interferon alfa-2a, interferon alfa-2b, interferon beta-1a, interferon beta-1b.

Note: In interferon nomenclature, the alfa, beta, gamma... designation refer to interferons with different amino acid sequence, while in INN of other substances the Greek letters refer to differential glycosylation.

albinterferon alfa-2b (99), *cepeginterferon alfa-2b* (105), *interferon alfa* (73), *interferon alfacon-1* (77), *interferon beta* (73), *interferon gamma* (73), *mipeginterferon alfa-2b* (114), *peginterferon alfa-2a* (84), *peginterferon alfa-2b* (84), *peginterferon alfacon-2* (116), *peginterferon beta-1a* (108), *peginterferon lambda-1a* (105), *ropeginterferon alfa-2b* (109), *sampeginterferon beta-1a* (116).

3.24. Interleukin receptor antagonists

The common stem for interleukin receptor antagonists is **-kinra**.

-nakinra for interleukin-1 (IL-1) receptor antagonists:

anakinra (72), *isunakinra* (113)

-trakinra for interleukin-4 (IL-4) receptor antagonists:

pittrakinra (87)

3.25. Interleukin type substances

The common stem for interleukin type substances is **-kin**.

For glycosylated interleukin type substances see item 2.2: General policies for glycosylated substances.

-nakin for interleukin-1 (IL-1) analogues and derivatives:

-onakin for interleukin-1 α analogues and derivatives:

pifonakin (77)

-benakin for interleukin-1 β analogues and derivatives:

mobenakin (72)

-leukin for interleukin-2 (IL-2) analogues and derivatives:

adargileukin alfa (89), aldesleukin (63), bempegaldesleukin (119), celmoleukin (65), cergutuzumab amunaleukin (113), denileukin diftitox (78), efavaleukin alfa (118), pegaldesleukin (74), teceleukin (67), tucotuzumab celmoleukin (95)

For interleukin-3 (IL-3) analogues and derivatives (see item 3.11).

-trakin for interleukin-4 (IL-4) analogues and derivatives:

binetrakin (82)

-exakin for interleukin-6 (IL-6) analogues and derivatives:

atexakin alfa (72)

-eptakin for interleukin-7 (IL-7) analogues and derivatives:

efineptakin alfa (118)

-octakin for interleukin-8 (IL-8) analogues and derivatives:

canoctakin (110), emoctakin (74)

-decakin for interleukin-10 (IL-10) analogues and derivatives:

ilodecakin (81), pegilodecakin (117)

-elvekin for interleukin-11 (IL-11) analogues and derivatives:

oprelvekin (76)

-dodekin for interleukin-12 (IL-12) analogues and derivatives:

edodekin alfa (79)

-tredekin for interleukin-13 (IL-13) analogues and derivatives:

cintredekin besudotox (92)

-octadekin for interleukin-18 (IL-18) analogues and derivatives:

iboctadekin (92)

-enicokin for interleukin-21 (IL-21) analogues and derivatives:

denenicokin (99)

Exceptions (interleukin type substances in which the preferred stem has not been used):

-plestim for interleukin-3 (IL-3) analogues and derivatives (see item 3.11).

-neurin for neurotrophins (interleukin-78, brain derived neurotropic factor; pre-stem, belongs to this group but in which the preferred stem has not been used):

abrineurin (84).

3.26. Monoclonal antibodies

The common stem for monoclonal antibodies is **-mab**.

For the General policy for monoclonal antibodies see item 2.9.

For glycosylated monoclonal antibodies see item 2.2: General policy for glycosylated substances.

INN for monoclonal antibodies alphabetically ordered by target class:

-ami- for **serum amyloid protein (SAP)/amyloidosis** (previously as *-am(i)-*):

birtamimab (119)

Under the previous naming scheme:

humanized: *-zumab*

dezamizumab (115)

-ba- for **bacterial** (previously as *-b(a)-*, *-ba(c)-*):

Under the previous naming scheme:

mouse: *-omab*

edobacomab (80)

chimeric: *-ximab*

pagibaximab (93)

humanized: -zumab

rivabazumab (114), rivabazumab pegol (113), tefibazumab (92)

human: -umab

nebacumab (66), panobacumab (100), raxibacumab (92)

-ci- for **cardiovascular** (previously as -c(i)-, -ci(r)-):

abelacimab (119), dilpacimab (119)¹⁴, faricimab (118)¹⁴, frovocimab (119), garadacimab (120), glenzocimab (120), marstacimab (119), nimacimab (120), olinvacimab (119), osocimab (119),

Under the previous naming scheme:

mouse: -omab

biciromab (66), imciromab (66)

chimeric: -ximab

abciximab (80), volociximab (93)

chimeric-humanized/human: -xizumab

navicixizumab (114)¹⁴

humanized: -zumab

alacizumab pegol (98), bevacizumab (86), bevacizumab beta (114), bococizumab (110), brolocizumab (112), caplacizumab (106), concizumab(108), demcizumab (107), emicizumab (113), etaracizumab (99), idarucizumab (115), lodelcizumab (108), ralpancizumab (110), tadocizumab (94), vanucizumab (113)¹⁴

human: -umab

alirocumab (107), ascrinvacumab (113), enoticumab (107), evinacumab (112), evolocumab (108), icrucumab (104), inclacumab (106), nesvacumab (108), orticumab (107), ramucirumab (110), rinucumab (113), varisacumab (116), vesencumab (104)

-de- for **metabolic or endocrine pathways**:

volagidemab (120)

Under the previous naming scheme:

human: -umab

crotedumab (114)

¹⁴ bi-specific monoclonal antibody.

-fung- for **fungal** (previously as *-f(u)-*):

Under the previous naming scheme:

human: *-umab*

efungumab (95)

-gros- for **skeletal muscle mass related growth factors and receptors** (pre-substem, previously as *-gr(o)-*):

Under the previous naming scheme:

humanized: *-zumab*

domagrozumab (114), *landogrozumab* (113)

human: *-umab*

bimagrumab (111), *trevogrumab* (113)

-ki- for **interleukin** (previously as *-k(i)-*, *-ki(n)-*):

abrezekimab (118), *bermekimab* (120), *cendakimab* (120), *etokimab* (120), *netakimab* (118), *romilkimab* (118)¹⁴

Under the previous naming scheme:

humanized: *-zumab*

anrukinzumab (98), *bimekizumab* (110), *clazakizumab* (107), *enokizumab* (104), *gevokizumab* (104), *ixekizumab* (105), *lebrikizumab* (101), *lutikizumab* (115), *mirikizumab* (117), *olokizumab* (103), *perakizumab* (108), *risankizumab* (113), *tildrakizumab* (108), *vnakizumab* (115)

human: *-umab*

afasevikumab (113), *brazikumab* (115), *briakinumab* (101), *canakinumab* (97), *dectrekumab* (112), *fezakinumab* (101), *fletikumab* (110), *guselkumab* (109), *secukinumab* (102), *sirukumab* (105), *tralokinumab* (102), *ustekinumab* (99)

-li- for **immunomodulating** (previously as *-l(i)-*, *-li(m)-*):

balstilimab (120), *bersanlimab* (118), *budigalimab* (119), *cemiplimab* (119), *cetrelimab* (118), *cobolimab* (120), *crovalimab* (119), *dostarlimab* (119), *envafolimab* (120), *etigilimab* (118), *ieramilimab* (120), *imaprelimab* (118), *iscalimab* (118), *leronlimab* (118), *levilimab* (120), *magrolimab* (120), *mitazalimab* (119), *nidanilimab* (120), *obexelimab* (119), *ontamalimab* (119), *onvatilimab* (118), *orilanolimab* (119), *otilimab* (119), *pozelimab* (120), *prolgolimab* (119), *quetmolimab* (120), *ravagalimab* (118), *relatlimab* (119), *sintilimab* (119), *spesolimab* (119), *sutimlimab* (118), *tavolimab* (118), *temelimab*

(119), tomaralimab (120), toripalimab (119), vopratelimab (118), zalifrelimab (120), zampilimab (119),

Under the previous naming scheme:

mouse: -omab

afelimomab (80), begelomab (111), dorlimomab aritox (66), elsilimomab (89), enlimomab (80), enlimomab pegol (77), faralimomab (81), gavilimomab (84), inolimomab (80), maslimomab (66), nerelimomab (81), odulimomab (81), telimomab aritox (66), vepalimomab (80), zolimomab aritox (80)

chimeric: -ximab

andecaliximab (115), basiliximab (81), clenoliximab (77), galiximab (89), infliximab (77), keliximab (81), lumiliximab (90), priliximab (80), teneliximab (87), vopaliximab (87)

chimeric-humanized/human: -xizumab

otelixizumab (99), rozanolixizumab (115)

humanized: -zumab

apolizumab (87), aselizumab (88), atezolizumab (112), benralizumab (102), cabiralizumab(114), camrelizumab (115), cedelizumab (81), certolizumab pegol (97), crizanlizumab (115), daclizumab (78), daclizumab beta (114), dapirolizumab pegol (110), eculizumab (87), efalizumab (85), erlizumab (84), etrolizumab (104), fontolizumab (87), ibalizumab (97), inebilizumab (113), itolizumab (103), lampalizumab (107), letolizumab (116), ligelizumab (107), lulizumab pegol (111), mepolizumab (81), mogamulizumab (104), monalizumab (113), natalizumab (79), nemolizumab (112), ocrelizumab (95), olendalizumab (116), omalizumab (84), ozoralizumab (105), pascolizumab (87), pateclizumab (105), pembrolizumab (110), pexelizumab (86), pidilizumab (108), plozalizumab (113), quilizumab (106), ravulizumab (117), reslizumab (85), rontalizumab (101), rovelizumab (81), ruplizumab (83), samalizumab (105), satralizumab (116), sipilizumab (87), spartalizumab (117), talizumab (89), teplizumab (97), tibulizumab (117)¹⁴, tislelizumab (117), tocilizumab (90), toralizumab (87), tregalizumab (104), vatelizumab (105), vedolizumab (100), visilizumab (84), vobarilizumab (114)¹⁴, vonlerolizumab (116)

human: -umab

abrilumab (111), adalimumab (85), adalimumab beta (118), anifrolumab (109), atorolimumab (80), avelumab (113), belimumab (89), bertilimumab (88), bleselumab (113), brodalumab (105), camidanlumab (117), camidanlumab tesirine (117), carlumab (104), dupilumab (108), durvalumab (112), eldelumab (109), emapalumab (116), foralumab (103), fresolimumab (101), gimsilumab (117), golimumab (91), ianalumab (117), imalumab (111), ipilimumab (94), lanadelumab (114), lenzilumab (111), lerdelimumab (86), lirilumab (107), mavrimumab (102), metelimumab (88), morolimumab (79), namilumab (104), nivolumab (111), oleclumab (116), oxelumab (105), pamrevlumab (113), placulumab (107), prezalumab (114), remtolimumab (115), sarilumab (106), selicrelumab (116), sifalimumab (104), stamulumab (95), tabalumab (105), tesidolumab (112), tezepelumab (113), timolumab (114), tiragolumab (117), tremelimumab (97), ulocuplumab (110), urelumab (104), utomilimumab (115), varlilumab (111), zanolimumab (92), ziralimumab (84)

-ne- for **neural** (previously as *-n(e)-*, *-ne(r)-*):

cinpanemab (120), *donanemab (120)*, *gosuranemab (119)*, *pepinemab (120)*,
semorinemab (120), *tilavonemab (120)*,

Under the previous naming scheme:

humanized: *-zumab*

bapineuzumab (93), *crenezumab (105)*, *eptinezumab (115)*, *fremanezumab (115)*,
galcanezumab(114)¹⁴, *ozanezumab (108)*, *ponezumab (104)*, *prasinezumab (117)*,
refanezumab (114), *solanezumab (107)*, *tanezumab (99)*

human: *-umab*

aducanumab (110), *atinumab (104)*, *elezanumab (115)*, *erenumab (115)*, *fasinumab (107)*,
fulranumab (104), *gantenerumab (108)*, *opicinumab (113)*

-os- for **bone** (previously as *-s(o)-*):

garetosmab (120)

Under the previous naming scheme:

humanized: *-zumab*

blosozumab (105), *romosozumab (106)*

human: *-umab*

burossumab (115), *denosumab (94)*, *setrusumab (117)*

-ta- for tumour (previous as *-t(u)-*, *-tu(m)-* ; *-co(l)-* ; *-go(t)-* ; *-go(v)-* ; *-ma(r)-* ; *-me(l)-* ;
pr(o)-):

belantamab (118), *belantamab mafodotin (118)*, *cibisatamab (118)¹⁴*, *disitamab (120)*,
disitamab vedotin (120), *enapotamab (118)*, *enapotamab vedotin (118)*, *gancotamab (119)*,
iodine (131I) apamistamab (119), *lacutamab (120)*, *murlentamab (119)*, *naxitamab (120)*,
omburtamab (119), *plamotamab (120)¹⁴*, *rolinsatamab (119)*, *rolinsatamab talirine (119)*,
samrotamab (118), *samrotamab vedotin (118)*, *serclutamab (120)*, *serclutamab talirine*
(120), *tafasitamab (119)*, *tamrintamab (120)*, *tamrintamab pamozirine (120)*, *teclistamab*
(120)¹⁴, *tepoditamab (118)¹⁴*, *tidutamab (120)¹⁴*, *vibecotamab (120)¹⁴*, *vofatamab (120)*,

Under the previous naming scheme:

mouse: *-omab*

abagovomab (95), *altumomab (80)*, *anatumomab mafenatox (86)*, *arcitumomab (74)*,
bectumomab (81), *blinatumomab (100)*, *capromab (80)*, *detumomab (80)*, *edrecolomab*
(74), *epitumomab (97)*, *epitumomab cituxetan (89)*, *ibritumomab tiuxetan (86)*, *igovomab*
(86), *lilotomab (112)*, *lutetium (¹⁷⁷Lu) lilotomab satetraxetan (112)*, *minretumomab (80)*,
mitumomab (82), *moxetumomab pasudotox (102)*, *nacolomab tafenatox (80)*, *naptumomab*

estafenatox (96), oregovomab (86), racotumomab (100), satumomab (81), solitomab (106), taplitumomab paptax (84), technetium (^{99m}Tc) nofetumomab merpentan (81), technetium (^{99m}Tc) pintumomab (86), tenatumomab (99), tositumomab (80)

chimeric: -ximab

amatuximab (104), bavituximab (95), brentuximab vedotin (103), carotuximab (114), cetuximab (82), cetuximab sarotalocan (120), coltuximab ravtansine (109), dinutuximab (109), dinutuximab beta (113), ecromeximab (87), ensituximab (103), futuximab (107), girentuximab (101), indatuximab ravtansine (105), iodine (^{131}I) derlotuximab biotin (113), iodine (^{124}I) girentuximab (101), isatuximab (112), laprituximab (114), laprituximab emtansine (114), margetuximab (109), mirvetuximab (114), mirvetuximab soravtansine (113), modotuximab (110), naratuximab (114), naratuximab emtansine (114), rituximab (77), siltuximab (100), tabituximab (119), tabituximab barzuxetan (119), tomuzotuximab (118), ublituximab (104), vadastuximab (114), vadastuximab talirine (113)

chimeric-humanized/human: -xizumab

azintuxizumab (116), azintuxizumab vedotin (116), depatuxizumab (115), depatuxizumab mafodotin (115), duvortuxizumab (116), losatuxizumab (116), losatuxizumab vedotin (116), ontuxizumab (109), pasotuxizumab (111),

humanized: -zumab

abitudzumab (109), alemtuzumab (83), bemaritudzumab (117), bivitudzumab (86), brontictuzumab (111), cantuzumab mertansine (105), cantuzumab ravtansine (105), cergutuzumab amunaleukin (113), citatuzumab bogatox (99), clivatuzumab tetraxetan (113), codrituzumab (109), cofetuzumab (117), cofetuzumab pelidotin (117), cusatuzumab (118), dacetuzumab (98), dalotuzumab (107), denintuzumab mafodotin (111), diligotuzumab (110), elotuzumab (100), emactuzumab (111), emibetuzumab (111), enavitudzumab (104), enoblitudzumab (116), epratuzumab (82), farletuzumab (100), ficlatuzumab (105), flotetuzumab (118)¹⁴, gatipotuzumab (118), gemituzumab (83), gemituzumab ozogamicin (115), ifabotuzumab (115), iladatuzumab (117), iladatuzumab vedotin (117), ingatuzumab (107), inotuzumab ozogamicin (92), labetuzumab (85), labetuzumab govitecan (113), lacnotuzumab (116), ladiratuzumab (117), ladiratuzumab vedotin (117), lifastuzumab vedotin (110), lintuzumab (86), lorvotuzumab mertansine (103), lumretuzumab (111), matuzumab (88), milatuzumab (98), mosunetuzumab (117)¹⁴, nimotuzumab (94), obinutuzumab (109), ocaratuzumab (107), onartuzumab (104), oportuzumab monatox (100), otlertuzumab (110), parsatuzumab (107), pertuzumab (89), pinatuzumab vedotin (108), polatuzumab vedotin (110), rosmantuzumab (115), rovalpituzumab (113), rovalpituzumab tesirine (113), sacituzumab (115), sacituzumab govitecan (113), sibrotuzumab (86), simtuzumab (107), sofituzumab vedotin (110), sontuzumab (94), talacotuzumab (117), telisotuzumab (115), telisotuzumab vedotin (115), tigatuzumab (98), timigutuzumab (118), trastuzumab (78), trastuzumab beta (118), trastuzumab deruxetecan (116), trastuzumab duocarmazine (115), trastuzumab emtansine (103), tucotuzumab celmoleukin (95), vandortuzumab vedotin (112), veltuzumab (98), vorsetuzumab (107), vorsetuzumab mafodotin (107), xentuzumab (114)¹⁴, yttrium (^{90}Y) clivatuzumab tetraxetan (102), yttrium ^{90}Y tacatuzumab tetraxetan (93), zenocutuzumab (118)¹⁴

human: -umab

adecatumumab (90), anetumab ravtansine (109), aprutumab (115), aprutumab ixadotin (115), cixutumumab (100), conatumumab (99), daratumumab (101), drozitumab (103), dusigitumab (108), elgemtumab (112), enfortumab vedotin (109), figitumumab (100), flinvotumab (106), ganitumab (103), glembatumumab (102), glembatumumab vedotin (113), indusatumab (112), indusatumab vedotin (112), intetumumab (101), iratumumab (94), istiratumab (117)¹⁴, lexatumumab (95), loncastuximab (117), loncastuximab tesirine (117), lucatumumab (98), lupartumab (115), lupartumab amadotin (115), mapatumumab (93), narnatumab (105), necitumumab (100), ofatumumab (93), olaratumab (103), panitumumab (96), patritumab (106), pritumumab (89), radretumab (104), rilatumumab (101), robatumumab (100), seribantumab (108), sirtratumab (117), sirtratumab vedotin (117), tarextumab (109), teprotumumab (108), tisotumab (113), tisotumab vedotin (113), tovetumab (109), vantictumab (109), votumumab (80), zalutumumab (93), zolbetuximab (117)

-toxa- for **toxin** (previously as -tox(a)-):

Under the previous naming scheme:

chimeric: -ximab

obilttoxaximab (113), pritoxaximab (108), setoxaximab (108)

humanized: -zumab

urtoxazumab (90)

human: -umab

actoxumab (111), atidortoxumab (117), berlimatoxumab (117), bezlotoxumab (107), suvratoxumab (116), tosatoxumab (109)

-vetmab for **veterinary use**:

bedinvetmab (120), blontuветmab (114), frunevetmab (116), gilvetmab (116), lokivetmab (112), ranevetmab (115), relfovetmab (120), tamtuветmab (114)

-vi- for **viral** (previously as -v(i)-, -vi(r)-):

atoltivimab (120), elipovimab (120), lenvervimab (118), maftivimab (120), nirsevimab (119)

Under the previous naming scheme:

chimeric: -ximab

cosfroviximab (116), larcaviximab (116), porgaviximab (116)

humanized: -*zumab*

felvizumab (77), *motavizumab* (95), *palivizumab* (79), *suvizumab* (102)

human: -*umab*

diridavumab (111), *exbivirumab* (91), *firivumab* (111), *foravirumab* (100),
gedivumab (117), *lesofavumab* (117), *libivirumab* (91), *navivumab* (113), *rafivirumab*
(100), *regavirumab* (80), *sevirumab* (66), *suptavumab* (115), *tuvirumab* (66)

Others:

under-*le(s)*- for **inflammatory lesions** (infix no longer formally acknowledged under the current scheme):

mouse (under the previous naming scheme -*omab*):

besilesomab (92), *lemalesomab* (86), *sulesomab* (86), *technetium (^{99m}Tc) fanolesomab* (86)

humanized (under the previous naming scheme -*zumab*):

ranibizumab (90) (treatment of patients with the exudative (wet or neovascular) form of age-related macular degeneration (AMD))

rat-murine hybrid (under the previous naming scheme -*axomab*):

catumaxomab (93), *ertumaxomab* (93)

human (under the previous naming scheme -*umab*):

roledumab (103), (treatment of RhD(+) incompatible transfusions)

muromonab-CD3 (59) (the first monoclonal antibody to which an INN was assigned belongs to this group but it was named before the stem was established)

3.27. Oxytocin derivatives

The common stem for oxytocin derivatives is -*tocin*.

argiprestocin (13), *aspartocin* (11), *carbetocin* (45), *cargutocin* (35), *demoxytocin* (22),
merotocin (111), *nacartocin* (51), *oxytocin* (13).

3.28. Peptides and Glycopeptides

The common stem for peptides and glycopeptides is -*tide*.

For special groups of peptides see -*actide* (Synthetic polypeptides with a corticotropin-like action, item 3.33), -*pressin* (Vasoconstrictors, vasopressin derivatives, item 3.36), -*relin* (Pituitary hormone-release stimulating peptides, item 3.30), -*tocin* (Oxytocin derivatives, item 3.27)

Peptides and glycopeptides are organized by the mode of action or by therapeutic use. Substems and pre-stems exist for some categories.

-glutide for glucagon-like peptide (GLP) analogues:

albiglutide (97), apraglutide (120), beinaglutide (117), dulaglutide (103), elsiglutide (104), glepaglutide (116), liraglutide (87), semaglutide (101), taspoglutide (99), teduglutide (90)

-motide for peptides used for active immunization:

abecomotide (109), adegromotide (115), alicdamotide (109), amilomotide (105), asudemotide (107), baloramotide (120), disomotide (94), elpamotide (103), graunimotide (113), latromotide (107), nelatimotide (115), ovemotide (94), pradimotide (107), sultimotide alfa (117), tanurmotide (109), tecemotide (108), tertomotide (98), tiplimotide (82), trempamotide (107), zastumotide (110)

-pultide for peptides used in pulmonary surfactants:

elopultide (119), lusupultide (80), redipultide (119), sinapultide (78)

-reotide for somatostatin receptor agonists/antagonists:

depreotide (80), edotreotide (84), ilatreotide (68), lanreotide (64), lutetium (¹⁷⁷Lu) oxodotreotide (116), octreotide (52), pasireotide (90), pentetreotide (66), satoreotide (115), satoreotide tetraxetan (118), satoreotide trizoxetan (114), vapreotide (62), veldoreotide (117)

-ritide for natriuretic peptides:

anaritide (57), carperitide (65), cenderitide (105), neseritide (80), ularitide (69), vosoritide (112)

Others:

analgesic: *leconotide (86), ziconotide (78)*

angiogenesis inhibitor: *cilengitide (81)*

anti-inflammatory: *brimapitide (114), dusquetide (113), icrocaptide (89)*

antianaemic: *peginesatide (108)*

antidepressant: *nemifitide (87)*

antidiabetic: *albenatide (114), amlintide (76), bamadutide (119), cotadutide (119), davalintide (101), efinopegdutide (120), efpeglenatide (111), exenatide (89), livoletide (118), lixisenatide (99), pegapamodutide (116), pramlintide (74), seglitide (57), tirzepatide (120)*

antiviral: *bulevirtide (118), enfuvirtide (85), tifuvirtide (91)*

autoimmune disorders: *dalazatide (111), dirucotide (100)*

calcium sensing receptor agonist: *etelcalcetide (112)*

cardiovascular indications: *aclerastide* (110), *danegaptide* (101), *elamipretide* (113), *ensereptide* (107), *epitifibatide* (78), *mibenratide* (111), *rotigaptide* (94), *rusalattide* (96), *teprotide* (36)

chemokine CXCR4 receptor antagonist: *balixafortide* (112), *motixafortide* (120)

decoy receptor: *nangibotide* (117)

diagnostic: *betiatide* (58), *bibapcitide* (78), *ceruletide* (34), *depreotide* (80), *flotegatide* (¹⁸F) (108), *fluciclatide* (¹⁸F) (103), *maraciclatide* (103), *mertiattide* (60), *pegloprastide* (120), *pendetide* (70), *technetium* (^{99m}Tc) *apcitide* (86), *technetium* (^{99m}Tc) *etarfolattide* (107), *teriparatide* (50), *tozuleristide* (115)

expectorant (in cystic fibrosis): *lancovutide* (99)

gastrointestinal indications: *dolcanattide* (114), *lagattide* (75) (*antidiarrhoeal*), *larazottide* (99) (*zonulin antagonist in celiac disease*), *linaclottide* (97), *ociltide* (52) (*gut motility increasing*), *plecanattide* (104), *recanaclottide* (115), *sulglycotide* (29), *triletide* (50)

glucagon-like peptide-1 (GLP-1) receptor antagonist: *avexitide* (120)

growth stimulant (veterinary): *nosiheptide* (35)

hormone analogues: *abaloparatide* (109), *semparatide* (80), *teriparatide* (50) (see also category “diagnostic”)

immunological agents and antineoplastics: *almurtide* (74), *brimatide* (114); *delmitide* (92), *edratide* (89), *fexapotide* (114), *goralattide* (72), *mifamurtide* (95), *murabutide* (49), *paclitaxel trevatide* (109); *pentigetide* (60), *pimelautide* (53), *prezatide copper acetate* (67), *rolipoltide* (94), *romurtide* (61), *ruxotemittide* (119), *tabilautide* (60), *temurtide* (60), *tigapotide* (95), *vipivotide tetraxetan* (120)

kallikrein inhibitor: *ecallantide* (93)

melanocortin receptor agonists (-melano-): *afamelanottide* (99), *bremelanottide* (95), *modimelanottide* (111), *setmelanottide* (112)

neurological indications: *alirinetide* (117), *cibinetide* (114), *davunettide* (100), *doreptide* (59), *ebiratide* (56), *nerinetide* (119), *obinepitide* (96), *pareptide* (38), *trofinettide* (112), *vanuttide cridificar* (100)

sedative: *emideltide* (70)

sodium channel activator: *solnatide* (113)

transforming growth factor inhibitor: *disitertide* (99)

urokinase plasminogen activator receptor (uPAR) inhibitor: *cenupattide* (119)

high mobility group (HMG) protein B1 analogue: *redasemttide* (117)

3.29. Pituitary / Placental glycoprotein hormones

The names selected by the International Union of Pure and Applied Chemistry-International Union of Biochemistry (IUPAC-IUB) have, to date, been chosen for compounds with an amino acid sequence identical to that of the naturally occurring human hormones. Addition of a Greek letter as the second part of the name will allow differentiation of different glycosylation patterns for compounds produced by biotechnology (see item 2.2: General policy for glycosylated substances).

(-)*follitropin* (follicle-stimulating hormones (FSH)):

corifollitropin alfa (80), *follitropin alfa* (71), *follitropin beta* (75), *follitropin gamma* (106), *follitropin delta* (112), *follitropin epsilon* (115), *urofollitropin* (57), *varfollitropin alfa* (101)

-*gonadotropin* (gonadotropin):

chorionic gonadotrophin (1), *choriogonadotropin alfa* (76), *choriogonadotropin beta* (120), *serum gonadotrophin* (1),

(-)*lutropin* (luteinizing hormones (LH)):

lutropin alfa (71)

3.30. Pituitary hormone-release stimulating peptides

The common stem for pituitary hormone-release stimulating peptides is **-*relin***.

luteinizing hormone–releasing hormone (LHRH)-release-stimulating peptides:

avorelin (74), *buserelin* (36), *deslorelin* (61), *fertirelin* (42), *gonadorelin* (32), *goserelin* (55), *histrelin* (53), *leuprorelin* (47), *lutrelin* (51), *nafarelin* (50), *peforelin* (93), *triptorelin* (58), *zoptarelin doxorubicin* (107)

-*morelin* for growth hormone (GH) release-stimulating peptides:

anamorelin (97), *capromorelin* (83), *dumorelin* (59), *examorelin* (72), *ipamorelin* (78), *lenomorelin* (106), *macimorelin* (100), *pralmorelin* (77), *rismorelin* (74), *sermorelin* (56), *somatorelin* (57), *tabimorelin* (86), *tesamorelin* (96), *ulimorelin* (103)

-*tirelin* for thyrotropin releasing hormone analogues:

azetirelin (60), *montirelin* (58), *orotirelin* (58), *posatirelin* (60), *protirelin* (31), *taltirelin* (75)

Exception:

thyrotropin alfa (78) (thyrotropin releasing hormone (TRH) analog, belongs to this group but in which the preferred stem has not been used)

Others:

cortimorelin (66) (diagnostic agent)

3.31. Receptor molecules or membrane ligands, native or modified

The stem for receptor molecules or membrane ligands, native or modified is **-cept**.

A preceding infix should designate the receptor type.

For glycosylated receptor molecules or membrane ligands, native or modified see item 2.2: General policy for glycosylated substances.

-ba- (B-cell activating factor receptors):

briobacept (98)¹⁵

-ber- (vascular endothelial growth factor receptors):

aflibercept (96)¹⁵, conbercept (105)¹⁵

-co- (complement receptors):

mirococept (91)

-far- (subgroup of interferon receptors):

bifarcept (86)

-fri- (frizzled family receptors):

ipafricept (109)¹⁵

-ki- (interleukin receptors):

inbakicept (120)¹⁵, olamkicept (116)¹⁵

-lefa- (CD58 (lymphocyte function-associated antigen 3, LFA-3)):

alefacept (84)¹⁵

-na- (interleukin-1 receptors):

rilonacept (95)¹⁵

-ner- (tumour necrosis factor (TNF) receptors):

asunercept (114)¹⁵, baminercept (99)¹⁵, etanercept (81)¹⁵, lenercept (72)¹⁵, onercept (86), opinercept (118)¹⁵, pegsunercept (95), tanfanercept (120), tulinercept (116)¹⁵

-ta- (CTLA4 (cytotoxic T-lymphocyte associated protein 4)):

abatacept (91)¹⁵, belatacept (93)¹⁵

-taci- (transmembrane activator and calcium modulator and cyclophilin ligand interactor):

atacept (95)¹⁵, telitacicept (120)¹⁵

¹⁵ Fc-fusion receptor molecules or membrane ligands, native or modified.

-ter- (transforming growth factor receptors):

dalantercept (105)¹⁵, luspatercept (110)¹⁵, ramatercept (108)¹⁵, sotatercept (104)¹⁵, talditercept alfa (119)¹⁵

-vir- (antiviral receptors):

alvircept sudotox (69)

Others:

valziflocept (117) (human low affinity IgG Fc receptor II-b peptide)

3.32. Small interfering RNAs¹⁶

The common stem for small interfering RNAs is **-siran**.

asvasiran (111), bamosiran (106), bevasiranib (108), cemdisiran (114), cosdosiran (116), fitusiran (113), givosiran (114), inclisiran (115), lumasiran (117), patisiran, (118), revusiran (111), teprasiran (116), tivanisiran (117), vutrisiran (119)

3.33. Synthetic polypeptides with a corticotropin-like action

The common stem for synthetic polypeptides with a corticotropin-like action is **-actide**.

alsactide (45), codactide (24), giractide (29), norleusactide (18), seractide (31), tetracosactide (18), tosactide (24), tricosactide (44), tridecactide (97)

3.34. Thrombomodulins

sothrombomodulin alfa (101), thrombomodulin alfa (94)

3.35. Toxins

aviscumine (86) (toxin ML-1 (mistletoe lectin I) (*Viscum album*))

3.36. Vasoconstrictors, vasopressin derivatives

The common stem for vasoconstrictors, vasopressin derivatives is **-pressin**.

argipressin (13), desmopressin (33), felypressin (13), lyppressin (13), ornipressin (22), selepressin (105), terlipressin (46), vasopressin injection (16)

¹⁶ For antisense oligonucleotides see item 3.2 and for various see item 3.38.

3.37. Vaccine-like substances (eg. peptide vaccines, recombinant vaccines)

Definition of peptide vaccines: vaccine in which antigens are produced from synthetic peptides, in order to stimulate an immune response.

Definition of recombinant vaccines: vaccine in which the antigen is derived by recombinant DNA technology. This may involve the isolation of a gene for a protein antigen and its expression to produce large quantities of the antigen (recombinant protein vaccine), or it may involve the construction of a genetically modified micro-organism (recombinant viral/bacterial vaccine).

- Peptides used for active immunization: **-motide** (see item 3.28).
- Recombinant vaccine:
 - verpasep caltespen (95)* (heat-shock protein HSP 65 (Mycobacterium bovis strain BCG) fusion protein with transcription factor E7 (human papilloma virus 16))

The suffix **-tespen** is used as indicator of heat shock protein.

- mRNA molecules used for active immunization:
 - nadorameran (113)* (an mRNA molecule encoding the rabies virus glycoprotein RAV-G containing elements for expression within eukaryotic cells; manufactured by enzymatic *in vitro* transcription from linearized plasmid DNA (*immunological agent for active immunization (antirabies)*))

3.38. Various¹⁷

Albumin-based substances:

iodinated (¹²⁵I) human serum albumin (24) (human serum albumin iodinated with radioactive iodine (¹²⁵I))

iodinated (¹³¹I) human serum albumin (24) (human serum albumin iodinated with radioactive iodine (¹³¹I))

macrosalb (¹³¹I) (33) (macroaggregated iodinated (¹³¹I) human albumin)

macrosalb (^{99m}Tc)(33) (technetium (^{99m}Tc) labelled macroaggregated human serum albumin)

ovandrotone albumin (52) (3-[(3,17-dioxoandrost-4-en-7 α -yl)thio]propionic acid, serum albumin conjugate)

Hemoglobin-based substances:

hemoglobin betafumaril (bovine) (115) ($S^3.\beta^{92}, S^3.\beta^{92}$ -bis(2-amino-2-oxoethyl)- $N^{6.\beta^{81}}, N^{6.\beta^{81}}$ -[(2E)-(but-2-enediyl)]bovine hemoglobin ($\alpha_2\beta_2$ tetramer))

hemoglobin crosfumaril (76) (hemoglobin A₀ (human $\alpha_2\beta_2$ tetrameric subunit), α -chain 99,99'-diamide with fumaric acid)

hemoglobin crosfumaril (bovine) (108) ($S^3.\beta^{92}, S^3.\beta^{92}$ -bis(2-amino-2-oxoethyl)- $N^{6.\alpha^{99}}, N^{6.\alpha^{99}}$ -(but-2-enediyl)bovine hemoglobulin ($\alpha_2\beta_2$ tetramer))

hemoglobin glutamer (80) (the species specificity should be indicated in brackets behind the name, "(bovine)"; the average mass of the polymer is given as e.g. haemoglobin glutamer-250 for 250kD)

hemoglobin raffimer (89) (The polyaldehyde [(2R,4S,6R,8R,11S,13R)-1,14-dihydroxy-4-hydroxymethyl-3,5,7,10,12-pentaoxatetradecane-2,4,6,8,11,13-hexacarbalddehyde] derived from raffinose [β -D-fructofuranosyl α -D-galactopyranosyl-(1 \rightarrow 6)- α -D-glucopyranoside] by treatment with sodium periodate is reacted with human hemoglobin A₀ at the 2,3-DPG binding pocket)

Hormone-based substances:

calcitonin (80) (a polypeptide hormone that lowers the calcium concentration in blood (the species specificity should be indicated in brackets behind the name))

parathyroid hormone (90) (non glycosylated human parathyroid hormone, the origin should be indicated between brackets after the INN, for example (r. *E. coli*) for recombinant produced by *Escherichia coli*)

¹⁷ The descriptions following the INN names may not be the complete definitions as shown in the publications of INN Lists.

secretin (01) (hormone of the duodenal mucosa which activates the pancreatic secretion and lowers the blood-sugar level)

secretin human (106) (human peptide hormone secretin)

serelaxin (105) (human relaxin 2 (relaxin H2))

Nucleotide-based substances¹⁸:

bazlitoranum (114) (DNA oligonucleotide that targets toll-like receptors; *-toran* USAN stem for TLR4 antagonists)

brivoligide (117) (23 bp decoy DNA; *-oligide* suffix for “OLIGonucleotIDE”)

defibrotide (44) (polydeoxyribonucleotides derived from mammalian lung with molecular weights ranging between 45.000 and 55.000 Da)

edifoligide (89) (14 bp decoy DNA; *-oligide* suffix for “OLIGonucleotIDE”)

etidalgide (119) (*all-P-ambo-5'-O-{(4RS)-1-[5'-O-{19-[(cholest-5-en-3 β -yl)oxy]-1-hydroxy-1,19-dioxo-2,5,8,11,14-pentaoxa-18-aza-1 λ^5 -phosphanadecan-1-yl}deoxy([1,2,3]tri-*P*-thio)(5'-GCTGTGCCCA CAACCCAGCA AACAAGCCTA GA-3')-3'-O-yl]-1,4,23-trihydroxy-1,11,23-trioxo-2,6,22-trioxa-10-aza-1 λ^5 ,23 λ^5 -diphosphatricosan-23-yl}deoxy([29,30,31]tri-*P*-thio)(5'-TCTAGGCTTG TTTGCTGGGT TGTGGGCACA GC-3')*)

imetelstat (101) (oligonucleotide; *-stat* stem for enzyme inhibitors)

rosomidnar (115) (DNA oligonucleotide sequence that is complementary to a region upstream of the B-cell lymphoma (BCL-2) gene)

Protein or peptide-based substances:

difelikefalin (113) ((pentapeptide, kappa opiate agonist)4-amino-1-(D-phenylalanyl-D-phenylalanyl-D-leucyl-D-lysyl)piperidine-4-carboxylic acid)

dasiglucagon (117) (mutated human glucagon analogue: [16-(2-methylalanine)(S>X),17-l-alanine(R>A),20-l- α -glutamyl(Q>E),21-l- α -glutamyl(D>E),24-l-lysyl(Q>K),27-l- α -glutamyl(M>E),28-l-serine(N>S)]human glucagon)

irop lact (74) (*N*-L-methionyl blood platelet factor 4 (human subunit))

metenkefalin (97) (L-tyrosylglycylglycyl-L-phenylalanyl-L-methionine- β -endorphin human-(1-5)-peptide)

mirostipen (85) ([23-methionine] human myeloid progenitor inhibitory factor 1-(23-99)-peptide)

¹⁸ For antisense oligonucleotides see item 3.2, for aptamers see item 3.4 and for small interfering RNA see item 3.32.

pegdinetanib (103) (94 residues protein derived from human fibronectin 10th type III domain, pegylated) (-*anib* stem for angiogenesis inhibitor)

talactoferrin alfa (93) (recombinant human lactoferrin)

tadekinig alfa (90) (interleukin-18 binding protein (human gene IL 18BP isoform a precursor))

thymalfasin (77) (synthetic thymosin alpha 1)

timbetasin (118) (thymosin β 4 analogue)

tiprelestat (103) (human elafin (elastase-specific inhibitor, skin-derived antileukoproteinase, peptidase inhibitor 3)) (-*stat* stem for enzyme inhibitors)

topsalysin (111) (recombinant DNA derived proaerolysin, pore-forming protein, from *Aeromonas hydrophila*, with the furin site substituted with a prostate specific antigen (PSA) cleavage site, fusion protein with 6 histidines, produced in *Escherichia coli* (nonglycosylated))

torapsel (91) (42-89-glycoprotein (human clone PMT21:PL85 P-selectin glycoprotein ligand 1) fusion protein with immunoglobulin (human constant region))

trebananib (106) (immunoglobulin G1 Fc fragment fused with two synthetic polypeptides that bind the *Homo sapiens* ANGPT2 (angiopoietin 2)) (-*anib* stem for angiogenesis inhibitor)

tremacamra (78) (1-453-glycoprotein ICAM-I (human reduced))

votucalis (96) (methionyl[145-leucine]FS-HBP2 (*Rhipicephalus appendiculatus* (Brown ear tick) Female-Specific Histamine-Binding Protein 2))

Others:

abicipar pegol (108) (pegylated composite protein for clinical applications (CPCA), with alternative scaffold domain to antigen receptors based on ankyrin repeats, anti-[*Homo sapiens* VEGFA (vascular endothelial growth factor A, VEGF-A, VEGF)]; glycyl-seryl-ankyrin repeats (3-35, 36-68, 69-101, 102-123)-lysylalanyl-bis(triglycyl-seryl) linker (127-134)-cysteinyl (1-135), conjugated via a maleimide group linker (thioether bond to C135) to a single linear methoxy polyethylene glycol 20 (mPEG20))

alisporivir (100) ([8-(*N*-methyl-D-alanine),9-(*N*-ethyl-L-valine)]cyclosporine)

andexanet alfa (110) (factor Xa inhibitors' neutralizing agent; des-(6-39)-human blood-coagulation factor X light chain (98-108')-disulfide with [185'-alanine (S>A)]human activated factor Xa heavy chain, produced in Chinese hamster ovary (CHO) cells (glycoform alfa))

angiotensin II (65) (5-L-isoleucineangiotensin II (the source of the material should be indicated))

angiotensinamide (12) (*N*-{1-{*N*-{*N*-{*N*-[*N*-(*N*²-asparaginylarginyl)valyl]tyrosyl}valyl}histidyl}prolyl}-3-phenylalanine)

conestat alfa (107) (human plasma protease C1 inhibitor (C1 esterase inhibitor) (*N,O*-glycosylated recombinant protein expressed in the mammary gland of transgenic rabbits), glycoform α) (*-stat* stem for enzyme inhibitors)

delcasertib (105) (human immunodeficiency virus 1 protein Tat-(46-57)-peptide (1→1')-disulfide with L-cysteinyl-[mouse protein kinase C delta type-(8-17)-peptide]) (*-sertib* stem for serine/threonine kinase inhibitor)

dianexin (109) (recombinant DNA derived annexin A5 dimer covalently linked by a 14 residues peptide linker, produced in *Escherichia coli* (nonglycosylated))

epelestat (92) (human recombinant neutrophil elastase inhibitor, bovine pancreatic trypsin inhibitor (BPTI) homologue) (*-stat* stem for enzyme inhibitors)

ismomultin alfa (91) (47-261-Glycoprotein gp 39 (human clone CDM8-gp39 reduced))

metreleptin (82) (*N*-methionylleptin (human))

murepavadin (113) (macrocyclic peptidomimetic, synthetic antibiotic)

nagrestipen (76) (macrophage inflammatory 1- α ; 26-L-alaninelymphokine MIP 1 α (human clone pAT464 macrophage inflammatory))

nomacopan (119) (complement factor C5 inhibitor)

opebacan (83) (132-L-alanine-1-193-bactericidal / permeability-increasing protein (human))

pegcetacoplan (120) (complement C3 inhibitor)

zilucoplan (118) (complement C5 inhibitor)

CURRENT CHALLENGES

The challenges currently faced by the INN Expert Group include:

- The use of a Biological Qualifier separate from the INN scheme to identify the source of a biological substance to enable substances to be traced in different licensing systems, whether classified as ‘similar biological substances’ or not.
- Formulation of policies for naming fusion proteins constructed from combination of different gene sequences as opposed to a natural protein from a single gene sequence.
- Various aspects of nomenclature of monoclonal antibodies (mAbs):
 - Simplification of the current system that has become overcrowded, for example by omitting the infix for source;
 - Policy for a scheme for nomenclature of glycosylated mAbs.
- The benefit of extending the INN system to mixtures and less well defined biological substances and therefore modifying the General Principles for biologicals.
- Development of a nomenclature scheme to clarify vaccines containing viruses and bacteria that could be assigned INN, including prophylactic vaccines that are currently assigned INN.
- If appropriate, extending the INN scheme to nomenclature of mixtures used for cell therapy and harmonizing to the extent possible with existing nomenclature systems for these products.

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** These documents are available on the INN Programme Website at:
<http://www.who.int/medicines/services/inn/en/>.*

ANNEX 1 .

List of INN for fusion proteins with one pharmacologically active component^{19, 20}

(this list excludes the INN ending with *-fusp*)

classified by groups

alb- (*human serum albumin*)

alb- & -cog

albutrepenonacog alfa (109)

human coagulation factor IX (EC 3.4.21.22, Christmas factor, plasma thromboplastin component) 148-threonine variant fusion protein with prolyl(human coagulation factor IX 148-threonine variant-(137-153)-peptide) fusion protein with human serum albumin, produced in CHO cells (alfa glycoform)

alb- & -interferon

albinterferon alfa-2b (99)

human serum albumin (585 residues) fusion protein with human interferon α -2b (165 residues)

alb- & -tide

albenatide (111)

$S^{3,34}$ -{1-[(23*S*)-23-{[exendin-4 *Heloderma suspectum* precursor-(48-86)-peptidyl (exenatidyl)]amino}-3,12,24-trioxo-7,10-dioxa-4,13,18,25-tetraazapentacosyl]-2,5-dioxopyrrolidin-3-yl}human serum albumin.

Peptide is synthetic, and human serum albumin is produced in *Saccharomyces cerevisiae*.

albiglutide (97)

[8-glycine]human glucagon-like peptide 1-(7-36)-peptidyl([8-glycine]human glucagon-like peptide 1-(7-36)-peptidyl)(human serum albumin (585 residues)

alb- & -som-

albusomatropin (114)

human serum albumin (residues 1-585) fusion protein with human somatotropin (growth hormone) (residues 586-776), produced in yeast cells (*Saccharomyces cerevisiae*) growth hormone derivative

¹⁹ A protein encoded from one nucleotide sequence generated from two or more genes - and possibly linkers - that originally encoded separate proteins.

²⁰ It should be noted that this list may not be comprehensive. The descriptions under the names are the published ones.

Others:

-al- & -grastim

balugrastim (107)

human serum albumin (585 residues) fusion protein with des-(1-alanine,37-valine,38-serine,39-glutamic acid)-human granulocyte colony-stimulating factor (pluripoietin)

-ase

asfotase alfa (104)²¹

tissue-nonspecific alkaline phosphatase- IgG₁ fusion protein;human tissue-nonspecific isozyme alkaline phosphatase (AP-TNAP, EC=3.1.3.1) fusion protein with leucyl-lysyl-human immunoglobulin G1 Fc region {(6-15)-H-CH₂-CH₃ of IGHG1*03} fusion protein with aspartyl-isoleucyl-deca(aspartic acid), dimer (493-493':496-496')-bisdisulfide

revelucosidase alfa (111)

des-(2-7)-human insulin-like growth factor II fusion protein with glycyl-L-alanyl-L-prolyl-human lysosomal alpha-glucosidase (acid maltase, aglucosidase alfa) produced in Chinese hamster ovary (CHO) cells, glycoform alfa

senrebotase (107)

L-methionylglycyl-L-seryl-des-(445-glycine,446-L-tyrosine)-[2-L-glutamic acid,432,442,444,447-tetra-L-aspartic acid]botulinum neurotoxin A precursor 27-L-alanine variant light chain (433-41')-disulfide with [14-L-arginine,15-L-lysine]human nociceptin fusion protein with L-alanyl-L-leucyl-L-alanyltris(tetraglycyl-L-seryl)-[3-L-valine,4-L-leucine,5-L-glutamine-418-L-leucine,419-L-aspartic acid]botulinum neurotoxin A heavy chain-(1-419)-peptide

tralesinidase alfa (117)

human α -N-acetylglucosaminidase fused to truncated human insulin-like growth factor II (IGF2) via a peptide linker, produced in Chinese hamster ovary (CHO) cells, glycoform alfa; human α -N-acetylglucosaminidase (NAG, EC=3.2.1.50) (1-720) fusion protein with glycyl-l-alanyl-l-prolyl-triglycyl-l-seryl-bis(1-prolyl-l-alanyl-l-prolyl-l-alanyl-l-prolyl-l-threonyl)-bis(1-prolyl-l-alanyl)-triglycyl-l-prolyl-l-seryl-glycyl-l-alanyl-l-prolyl-[37-l-alanine(R³⁷>A₍₇₈₁₎)]human insulin-like growth factor II (somatomedin-A, T3M-11-derived growth factor, IGF-II) (8-67)-peptide (752-811), produced in Chinese hamster ovary (CHO) cells, glycoform alfa

-cept

abatacept (91)

1-25-oncostatin M (human precursor) fusion protein with CTLA-4 (antigen) (human) fusion protein with immunoglobulin G1 (human heavy chain fragment), bimolecular (146→146')-disulfide

aflibercept (96)

des-432-lysine-[human vascular endothelial growth factor receptor 1-(103-204)-peptide (containing Ig like C2 type 2 domain) fusion protein with human vascular endothelial growth factor receptor 2-(206-308)-peptide (containing Ig like C2 type 3 domain

²¹ INN selected before the implementation of the *ef*- suffix.

fragment) fusion protein with human immunoglobulin G1-(227 C-terminal residues)-peptide (Fc fragment)], (211-211':214-214')-bisdisulfide dimer

alefacept (84)

1-92-antigen LFA-3 (human) fusion protein with human immunoglobulin G1 (hinge-CH₂-CH₃ γ 1-chain), dimer

asunercept (114)

fusion protein for immune applications (FPIA) comprising the *Homo sapiens* FAS (Fas cell surface death receptor, TNFRSF6, tumor necrosis factor receptor (TNFR) superfamily member 6, FAS1, APO-1, CD95) extracellular domain, fused with *Homo sapiens* immunoglobulin G1 Fc fragment;

Homo sapiens FAS precursor fragment 26-172 (1-147) -gamma1 chain H-CH₂-CH₃ fragment [Homo sapiens IGHG1*03 (hinge 5-15 (148-158), CH₂ (159-268), CH₃ (269-373), CHS (374-375))] (148-375); dimer (148-148':154-154':157-157')-trisdisulfide

atacicept (95)

[86-serine,101-glutamic acid,196-serine,197-serine,222-aspartic acid,224-leucine][human tumor necrosis factor receptor superfamily member 13B-(30-110)-peptide (TACI fragment containing TNFR-Cys 1 and TNFR-Cys 2) fusion protein with human immunoglobulin G1-(232 C-terminal residues)-peptide (γ 1-chain Fc fragment), (92-92':95-95')-bisdisulfide dimer

baminercept (99)

human tumor necrosis factor receptor superfamily member 3 (lymphotoxin- β receptor, TNF C receptor)-(2-195)-peptide (fragment of extracellular domain) fusion protein with human immunoglobulin heavy constant γ 1 chain Fc fragment [227 residues, hinge (195-205) des-(1-4),C5>V, CH₂ (206-315), CH₃ (316-421) des-K¹⁰⁷]

belatacept (93)

[Tyr²⁹,Glu¹⁰⁴,Gln¹²⁵,Ser¹³⁰,Ser¹³⁶,Ser¹³⁹,Ser¹⁴⁸](antigen CTLA-4 human-3-126]-peptide (fragment containing the human extracellular domain) fusion protein with immunoglobulin G1-[233 amino acids from the C-terminal of the heavy chain]-peptide (fragment containing the human monoclonal Fc domain), bimolecular (120 \rightarrow 120')-disulfide

briobacept (98)

aspartyl[1-valine,20-asparagine,27-proline](human tumor necrosis factor receptor superfamily member 13C (BAFF receptor, BlyS receptor 3 or CD268 antigen)-(1-71)-peptidyl (part of the extracellular domain))valyl(human immunoglobulin G1 Fc fragment, *Homo sapiens* IGHG1-(104-329)-peptide) (79-79':82-82')-bisdisulfide dimer

conbercept (105)

fusion protein for immune applications (FPIA) comprising *Homo sapiens* FLT1 (fms-related tyrosine kinase 1, vascular endothelial growth factor receptor 1, VEGFR1, vascular permeability factor receptor, tyrosine-protein kinase FRT) fragment, fused with *Homo sapiens* KDR (kinase insert domain receptor, vascular endothelial growth factor receptor 2, VEGFR2, protein-tyrosine kinase receptor FLK1, CD309) fragment, fused with *Homo sapiens* immunoglobulin G1 Fc fragment;
FLT1, 132-232 precursor fragment (1-101)-KDR, 227-421 precursor fragment (102-296) - glycyL-prolyl-glycyl (297-299) -gamma1 chain H-CH₂-CH₃ fragment (300-526) [*Homo sapiens* IGHG1*03 hinge 6-15 P13>L (307) (300-309), CH₂ (310-419), CH₃-CH-S (420-526)]; (305-305':308-308')-bisdisulfide dimer

dalantercept (105)

fusion protein for immune applications (FPIA) comprising *Homo sapiens* ACVRL1 (activin A receptor type II-like 1, activin receptor-like kinase 1, ALK1, ALK-1, serine/threonine-protein kinase receptor R3, SKR3, transforming growth factor-beta superfamily receptor type I, TGF-B superfamily receptor type I, TSR-I, HHT2, ORW2) fragment, fused with *Homo sapiens* immunoglobulin G1 Fc fragment;

ACVR2L1, 22-120 precursor fragment (1-99) -threonyl-triglycyl (100-103) -gamma1 chain H-CH2-CH3 fragment (104-328) [*Homo sapiens* IGHG1*03 hinge 8-15 (104-111), CH2 L1.3>A (115), G1>A (118), A115>V (211) (112-221), CH3 S85.3>P (284) (222-328)]; (107-107':110-110')-bisdisulfide dimer

etanercept (81)

1-235-tumor necrosis factor receptor (human) fusion protein with 236-467-immunoglobulin G1 (human γ 1-chain Fc fragment), dimer

inbakicept (120)

interleukin 15 receptor subunit alpha (human IL15R α) (1-65)-peptide (sushi domain-containing) fusion protein with human immunoglobulin G1 Fc fragment (232 C-terminal residues) (66-297) [*Homo sapiens* IGHG1*01, hinge (71-80), CH2 (81-190), CH3 (191-295), CHS (296-297)], (76-76':79-79')-bisdisulfide dimer, produced in Chinese hamster ovary (CHO) cells

ipafricept (109)

fusion protein for immune applications (FPIA) comprising *Homo sapiens* FZD8 (frizzled family receptor 8, Frizzled-8) extracellular domain, fused with *Homo sapiens* immunoglobulin G1 Fc fragment;

Homo sapiens FZD8 precursor fragment 28-158 (1-131) -*Homo sapiens* IGHG1*01 H-CH2-CH3 fragment (hinge 1-15 C5>S (136) (132-146), CH2 (147-256), CH3 (257-361), CHS (362-363)) (132-363); dimer (142-142':145-145')-bisdisulfide

lenercept (72)

1-182-tumor necrosis factor receptor (human reduced), (182→104')-protein with 104-330-immunoglobulin G1 (human clone pTJ5 C γ 1 reduced)

luspatercept (110)

fusion protein for immune applications (FPIA) comprising the *Homo sapiens* ACVR2B (activin receptor type 2B, activin A receptor type IIB, activin receptor type IIB, ACTR-IIB, ActR-IIB) extracellular domain, fused with *Homo sapiens* immunoglobulin G1 Fc fragment;

Homo sapiens ACVR2B precursor fragment 25-131 L79>D (55) (1-107) -linker triglycyl (108-110) -gamma1 chain H-CH2-CH3 fragment [*Homo sapiens* IGHG1*03 (hinge 8-15 (111-118), CH2 (119-228), CH3 (229-333), CHS (334-335))] (111-335); dimer (114-114':117-117')-bisdisulfide

olamkicept (116)

extracellular domains of glycoprotein 130 (gp130) fused to human immunoglobulin G1 Fc fragment, covalent dimer, produced in Chinese hamster ovary (CHO) cells;

human interleukin-6 receptor subunit beta (IL-6RB, interleukin-6 signal transducer, membrane glycoprotein 130, CD130 antigen) precursor-(23-617)-peptide fusion protein with [19-I-alanine(L>A(609)),20-I- α -glutamic acid(L>E(610)),22-I-alanine(G>A(612))]human immunoglobulin G1*03 Fc fragment-(6-232)-peptide, dimer (601-601':604-604')-bisdisulfide

opinercept (118)

human tumor necrosis factor receptor-2 extracellular domain (1-235) fused to a fragment of immunoglobulin G1 consisting of the Fc portion and hinge region (236-467), dimer, produced in Chinese hamster ovary (CHO) cells, glycosylated

ramatercept (108)

fusion protein for immune applications (FPIA) comprising *Homo sapiens* ACVR2B (activin A receptor type IIB, ActR-IIB) fragment, fused with *Homo sapiens* immunoglobulin G1 Fc fragment;

Homo sapiens ACVR2B precursor fragment 20-134 (1-115) -triglycyl (116-118) -*Homo sapiens* IGHG1*03 H-CH2-CH3 fragment (hinge 8-15 (119-126), CH2 A115>V (226) (127-236), CH3 (237-341), CHS (342-343)) (119-343); dimer (122-122':125-125')-bisdisulfide

rilonacept (95)

[653-glycine][human interleukin-1 receptor accessory protein-(1-339)-peptide (extracellular domain fragment) fusion protein with human type 1 interleukin-1 receptor-(5-316)-peptide (extracellular domain fragment) fusion protein with human immunoglobulin G1-(229 C-terminal residues)-peptide (Fc fragment)], (659-659':662-662')-bisdisulfide dimer

sotatercept (104)

fusion protein for immune applications (FPIA) comprising *Homo sapiens* ACVR2A (activin receptor type 2A, activin receptor type IIA) fragment fused with *Homo sapiens* immunoglobulin G1 Fc fragment;

Homo sapiens ACVR2A, 21-135 precursor fragment (1-115) -threonyl-triglycyl linker (116-119) -gamma1 chain H-CH2-CH3 fragment (120-344) [*Homo sapiens* IGHG1*03 hinge (120-127), CH2, A115>V (227) (128-237), CH3 (238-344)]; (123-123':126-126')-bisdisulfide dimer

telitacicept (120)

[L¹²⁰>A, L¹²¹>E, G¹²³>A, A²¹⁶>S, P²¹⁷>S]-TACI (transmembrane activator and CAML interactor, tumor necrosis factor receptor superfamily protein TNFRSF13B) human extracellular domain fragment (13-118)-peptide (1-106) fusion protein with human immunoglobulin G1-(227 C-terminal residues)-peptide (γ1-chain Fc fragment) (107-333) [*Homo sapiens* IGHG1*01, hinge (107-116), CH2 L¹²⁰>A, L¹²¹>E, G¹²³>A, A²¹⁶>S, P²¹⁷>S (117-226), CH3 (227-331), CHS (332-333)], (112-112':115-115')-bisdisulfide dimer, produced in Chinese hamster ovary (CHO) cells

tulinercept (116)

human tumor necrosis factor receptor superfamily member 1B (TNF receptor 2, TNF receptor II, p75, p80 TNF-alpha receptor, CD120b antigen)-(1-235)-peptide (extracellular domain), fusion protein with heavy chain constant region of the human immunoglobulin gamma1*03-(99-330)-peptide (Fc fragment) (236-467), fusion protein with C-terminal endoplasmic reticulum hexapeptide Ser-Glu-Lys-Asp-Glu-Leu; dimer (240-240':246-246':249-249')-trisdisulfide, produced in *Nicotiana tabacum* Bright Yellow-2 cells

-cept & -tox²² (-tox is for active toxins)

alvircept sudotox (69)

N²-L-methionyl-1-178-antigen CD4 (human clone pT4B protein moiety reduced)(178→248')-protein with 248-L-histidine-249- L-methionine-250- L-alanine-251- L-glutamic acid-248-613-exotoxin A(*Pseudomonas aeruginosa* reduced)

-imod

eftilagimod alfa (116)

human lymphocyte activation gene 3 protein extracellular domains fused to human immunoglobulin G1 Fc fragment through a linker peptide, covalent dimer, produced in Chinese hamster ovary (CHO) cells, glycoform alfa;

human lymphocyte activation gene 3 protein (LAG-3, protein FDC, CD223 antigen) precursor-(23-434)-peptidyltetrakis(l-α-aspartyl)-l-lysylbis(glycyl-l-seryl)glycylFc fragment of human immunoglobulin heavy constant G1*01, dimer (427-427':433-433':436-436')-trisdisulfide

efizonerimod alfa (117)

modified human immunoglobulin G4 Fc fragment fused to tumor necrosis factor receptor-associated factor TRAF2 (human C-C domain fragment) and to the CD252 antigen (human extracellular domain fragment), hexamer, produced in Chinese hamster ovary (CHO) cells,

²² The names and the descriptions of toxins are published in Annex 4.1 of "International Nonproprietary Names (INN) for pharmaceutical substances. Names for radicals, groups & others: comprehensive list (WHO/EMP/RHT/TSN/2015.1)".

glycoform alfa;
modified human immunoglobulin G4 Fc fragment (1-229) [*Homo sapiens* IGHG4*01 del-CH1, [10-proline (S>P)]hinge] fusion protein with human TNF receptor-associated factor2 (TRAF2)-(310-349)-peptide (230-269) fusion protein with des-(1-50)-human tumor necrosis factor ligand superfamily member4 (TNFSF4, also known as CD252 or OX40L) (270-402), produced in Chinese hamster ovary (CHO) cells, non-covalent trimer of (8-8',11-11')-bisdisulfide dimers, glycoform alfa

-kin

efineptakin alfa (118)

Met-Gly-Met (1-3)-human interleukin 7 (4-155) fused to an antibody hybrid fragment (hyFc) consisting of human immunoglobulin D (IgD) hinge and N-terminal CH2 regions (156-193) and human immunoglobulin G4 (IgG4) C-terminal CH2 and complete CH3 regions (194-400), dimer disulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

efavaleukin alfa (118)

immunoglobulin G1 γ 1-chain C-terminal constant region fragment (Fc) (1-226 without C-terminal Lys, N77G,D136E,L138M variant)-G₄S linker (227-231)-human interleukin 2 (232-364, V322K,C356A variant) fusion protein, dimer disulfide, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

-kin & -tox²²

cintredekin besudotox (92)

toxin hIL13-PE38QQR (plasmid phuIL13-Tx)

denileukin diftotox (78)

N-L-methionyl-387-L-histidine-388-L-alanine-1-388-toxin (*Corynebacterium diphtheriae* strain C7) (388→2')-protein with 2-133-interleukin 2 (human clone pTIL2-21a)

-mab & -kin

cergutuzumab amunaleukin (113)

immunoglobulin G1-kappa fused to IL2 (interleukin 2), anti-[*Homo sapiens* CEACAM5 (carcinoembryonic antigen-related cell adhesion molecule 5, CEA, CD66e)], humanized monoclonal antibody fused to IL2;
gamma1 heavy chain (1-451) [humanized VH (*Homo sapiens* IGHV1-18*01 (82.70%) - (IGHD)-IGHJ6*01) [8.8.14] (1-121) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (122-219), hinge (220-234), CH2 L1.3>A (238), L1.2>A (239), P114>G (333) (235-344), CH3 Y5>C (353), T22>S (370), L24>A (372), Y86>V (411) (345-449), CHS (450-451)) (122-451)], (224-215')-disulfide with kappa light chain (1'-215') [humanized V-KAPPA (*Homo sapiens* IGKV1-16*01 (82.10%) -IGKJ2*01) [6.3.10] (1'-108') -*Homo sapiens* IGKC*01, Km3 (109'-215')];
gamma1 heavy chain fused to IL2 (1"-598") [humanized VH (*Homo sapiens* IGHV1-18*01 (82.70%) - (IGHD)-IGHJ6*01) [8.8.14] (1"-121") -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (122"-219"), hinge (220"-234"), CH2 L1.3>A (238"), L1.2>A (239"), P114>G (333") (235"-344"), CH3 S10>C (358"), T22>W (370"), (345"-449"), CHS K2>del (450")) (122"-450") -15-mer (tris(tetraglycyl-seryl)) linker (451"-465") -*Homo sapiens* IL2 (Pr21-153) T23>A (468"), F62>A (507"), Y65>A (510"), L92>G (547"), C145>A (590") (466"-598")], (224"-215'")-disulfide with kappa light chain (1'"-215'") [humanized V-KAPPA (*Homo sapiens* IGKV1-16*01 (82.10%) -IGKJ2*01) [6.3.10] (1'"-108'") -*Homo sapiens* IGKC*01, Km3 (109'"-215'")];
dimer (230-230":233-233")-bisdisulfide

amunaleukin

tris[(tetraglycyl)seryl]-[3-alanine(T>A18),42-alanine(F>A57),45-alanine(Y>A60),72-glycine(L>G87),125-alanine(C>A140)]human interleukin-2 (IL-2, T-cell growth factor, TCGF)

tucotuzumab celmoleukin (95)

immunoglobulin G1, anti-(tumor associated calcium signal transducer 1 (KS 1/4 antigen)) (human-mouse monoclonal huKS-IL2 heavy chain) fusion protein with interleukin 2 (human), disulfide with human-mouse monoclonal huKS-IL2 light chain, dimer

celmoleukin (65)

interleukin 2 (human clone pTIL2-21a, protein moiety)

-mab & -tox²³ (-tox is for toxins (active or inactivated proteins))

anatumomab mafenatox (86)

immunoglobulin G 1, anti-(human tumor-associated glycoprotein 72) (human-mouse clone pMB125 Fab fragment γ 1-chain) fusion protein with enterotoxin A (227-alanine) (*Staphylococcus aureus*) complex with mouse clone pMB125 κ -chain)

citatumomab bogatox (99)

immunoglobulin Fab fusion protein, anti-[*Homo sapiens* tumor-associated calcium signal transducer 1 (TACSTD1, gastrointestinal tumor-associated protein 2, GA733-2, epithelial glycoprotein 2, EGP-2, epithelial cell adhesion molecule Ep-CAM, KSA, KS1/4 antigen, M4S, tumor antigen 17-1A, CD326)], humanized Fab fused with *Bougainvillea spectabilis* Willd rRNA N-glycosidase [type I ribosome inactivating protein (RIP), bouganin], VB6-845; gamma1 heavy chain fragment (1-225) [hexahistidyl (1-6) -humanized VH from 4D5MOC-B (*Homo sapiens* FR/*Mus musculus* CDR, *Homo sapiens* IGHJ4*01, V124>L) [8.8.9] (7-122) - *Homo sapiens* IGHG1*01 CH1-hinge fragment EPKSC (123-225)], (225-219')-disulfide with kappa fusion chain (1'-481') [humanized V-KAPPA from clone 4D5MOC-B (*Homo sapiens* FR/*Mus musculus* CDR, *Homo sapiens* IGKJ1*01, I126>L) [11.3.9] (1'-112') - *Homo sapiens* IGKC*01 (113'-219') -12-mer furin linker (proteolytic cleavage spacer from *Pseudomonas* exotoxin A) (220'-231') - *Bougainvillea spectabilis* Willd bouganin fragment (27-276 from precursor, V354>A, D358>A, Y364>N, I383>A) (232'-481')]

dorlimomab aritox (66)

ricin A chain-antibody ST 1 F(ab')₂ fragment immunotoxin

moxetumomab pasudotox (102)

immunoglobulin Fv fragment fused to *Pseudomonas* toxin, anti-[*Homo sapiens* CD22 (sialic acid-binding Ig-like lectin 2, Siglec-2, SIGLEC2, Leu-14, B-lymphocyte cell adhesion molecule, BL-CAM)], *Mus musculus* monoclonal antibody disulfide stabilized Fv fragment with the variable heavy VH domain fused with the truncated form PE38 of *Pseudomonas aeruginosa* exotoxin A (VH-PE38), disulfide linked with the variable kappa domain (V-KAPPA)];

VH-PE38 (1-476) comprising the VH domain (1-123) [methionyl -*Mus musculus* VH [(IGHV5-12-1*01 -(IGHD)-IGHJ3*01) [8.8.16] (2-123)] fused with a 7-mer linker (124-130) and with the *Pseudomonas aeruginosa* exotoxin A (ETA) PE38 fragment (131-476) [277-638 precursor fragment with del 389-405>N (131-476), containing domain II (131-243) with furin proteolytic cleavage site (152-164), domain Ib (244-267), domain III (268-476)], (45-101)-

²³ The names and the descriptions of toxins are published in Annex 4.1 of "International Nonproprietary Names (INN) for pharmaceutical substances. Names for radicals, groups & others: comprehensive list (WHO/EMP/RHT/TSN/2015.1)".

disulfide with V-KAPPA (1'-108') [methionyl -*Mus musculus* V-KAPPA [(IGHKV10-96*01 - IGKJ1*01) [6.3.9] (2'-108')]

nacolomab tafenatox (80)

immunoglobulin G1, anti-(human colorectal tumor antigen C242) Fab fragment (mouse monoclonal r-C242Fab-SEA clone pkP941 γ 1-chain) fusion protein with enterotoxin A (*Staphylococcus aureus*), disulfide with mouse monoclonal r-C242Fab-SEA clone pkP941 κ -chain

naptumomab estafenatox (96)

immunoglobulin fragment, anti-[trophoblast glycoprotein (TPBG, 5T4)] monoclonal 5T4 gamma1 heavy chain fragment fusion protein [*Mus musculus* VH (5T4V14: H41>P, S44>G, I69>T, V113>G)-IGHG1_CH1] - [Glycyl-Glycyl-Prolyl] - superantigen SEA/E-120 (synthetic), non-disulfide linked with monoclonal 5T4 kappa light chain [*Mus musculus* V-KAPPA (5T4V18: F10>S, T45>K, I63>S, F73>L, T77>S, L78>V, L83>A)-IGKC]

oportuzumab monatox (100)

immunoglobulin scFv fusion protein, anti-[*Homo sapiens* tumor-associated calcium signal transducer 1 (TACSTD1, gastrointestinal tumor-associated protein 2, GA733-2, epithelial glycoprotein 2, EGP- 2, epithelial cell adhesion molecule Ep-CAM, KSA, KS1/4 antigen, M4S1, tumor antigen 17-1A, CD326)] humanized monoclonal antibody scFv fused with *Pseudomonas aeruginosa* exotoxin A; hexahistidyl -humanized scFv [V-KAPPA (*Homo sapiens* IGKV1- 39*01 (78%)- IGKJ1*01, I126>L) [11.3.9] (7-118) -26-mer linker -VH (*Homo sapiens* IGHV7-4-1*02 -(IGHD)-IGHJ4*01, V124>L) [8.8.9] (145-260)] -20-mer linker - *Pseudomonas aeruginosa* exotoxin A (ETA) [277-633 precursor fragment, containing domain II (281-393) with furin proteolytic cleavage site (302-313), domain Ib (394-433), domain III (434-637)] (281-637) -hexahistidyl-lysyl-aspartyl-glutamylleucyl

taplitumomab paptox (84)

immunoglobulin G1, anti-(human antigen CD19) (mouse monoclonal B43 γ 1-chain), disulfide with mouse monoclonal B43 κ -chain, dimer, disulfide with protein PAP (pokeweed antiviral)

telimomab aritox (66)

ricin A chain-antibody T 101 Fab fragment immunotoxin

zolimomab aritox (80)

immunoglobulin G1, anti-(human CD5 (antigen) heavy chain) (mouse monoclonal H65-RTA γ 1-chain), disulfide with mouse monoclonal H65-RTA light chain, dimer, disulfide with ricin (castor bean A-chain)

som-

efpegsomatropin (113)

recombinant human growth hormone (somatropin) and human immunoglobulin G4 Fc fragment dimer, produced in *Escherichia coli* (nonglycosylated), linked together with polyethylene glycol derivative linker:

$N^{\alpha.1}, N^{1.1}$ -[ω -(oxypropane-1,3-diyl)- α -(propane-1,3-diyl)poly(oxyethylene)] human growth hormone, human immunoglobulin G4 Fc fragment (IGHG4*01 H-CH2-CH3)-(9'-229')-peptide dimer (3'-3'')-disulfide

eftansomatropin alfa (118)

human somatotropin (1-191) fused to a hybrid Fc consisting of human immunoglobulin D (IgD) hinge region, fused to the IgD N-terminal CH2 region (192-229), fused to the immunoglobulin G4 (IgG4) C-terminal CH2 region, fused to the IgG4 CH3 region (230-436), disulfide dimer, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

-tide

cenderitide (105)

natriuretic peptide receptor type B (NPR-B) agonist;
human C-type natriuretic peptide-(32-53)-peptide (CNP-22) fusion protein with eastern green mamba (*Dendroaspis angusticeps*) natriuretic peptide-(24-38)-peptide

dulaglutide (103)²⁴

glucagon-like peptide-1-immunoglobulin G4 fusion protein, [2-glycyl,16-l-glutamyl,30-glycyl][human glucagon-like peptide 1-(7-37)-peptide] {(8-A>G,22-G>E,36-R>G)-GLP-1(7-37)} fusion protein with tris(tetraglycyl-l-seryl)-l-alanine (linker) fusion protein with des-276-lysine-[57-l-proline,63-l-alanine,64-l-alanine]human immunoglobulin G4 Fc region {(10-S>P)-H-(4-F>A,5-L>A)-CH2-(107-K>-)-CH3 of IGHG4*01}, dimer (55-55':58-58')-bisdisulfide

efinopegdutide (118)

glucagon-like peptide-1 (GLP-1) analogue, conjugated by a 10 kDa polyethylene glycol (PEG) linker (n ~ 225) to an Fc portion dimer of human immunoglobulin G4 (IgG4):
 N^{1-1} -{3-[ω-(3-{3-[(3RS)-3-({16,20-anhydro-[Ser²>Aib,Ser¹⁶>Glu,Arg¹⁷>Lys,Gln²⁰>Lys,Asp²¹>Glu,Lys³⁰>Cys]-oxymodulin (1-30)-peptide 30-amide}-S^{3,30}-yl)-2,5-dioxopyrrolidin-1-yl]propanamido}propoxy)poly(oxyethylene)-α-yloxy]propyl}[immunoglobulin γ4 heavy chain constant region C-terminal 221-peptide dimer disulfide], non-glycosylated, immunoglobulin fragment dimer produced in *Escherichia coli*

efpeglenatide (111)

exenatide derivative and human IgG4 Fc dimer linked together with polyethylene glycol derivative:
 $N^{6,27},N^{1,9'}$ -[ω-(oxypropane-1,3-diyl)-α-(propane-1,3-diyl)poly(oxyethylene)] [1-(imidazol-4-ylacetic acid)]exenidin-4 *Heloderma suspectum* (Gila monster), human immunoglobulin G4 Fc fragment-(9'-229')-peptide dimer (11'-11'')-disulfide

elsiglutide (104)

[2-glycine(A>G),3-glutamic acid(D>E),8-serine(D>S),10-leucine(M>L),11-serine(N>S),16-alanine(N>A),24-alanine(N>A),28-alanine(Q>A)]human glucagon-like peptide 2 (GLP-2) fusion protein with hexalysinamide

glepaglutide (116)

mutated human glucagon like peptide-2 (GLP-2) analogue with a C-terminal hexa-lysine addition;
[2-glycine(A>G),3-glutamic acid(D>E),5-threonine(S>T),8-serine(D>S),10-leucine(M>L),11-alanine(N>A),16-alanine(N>A),24-alanine(N>A),28-alanine(Q>A)]human glucagon-like peptide 2 (GLP-2) fusion peptide with hexalysinamide

vanutide cridificar (100)²⁵

inactivated diphtheria toxin (carrier) covalently linked to human beta-amyloid protein 42 short fragments: pentadecakis[N^{6-Lys} -(sulfanylacetyl)]-[52-glutamic acid(G>E)]diphtheria toxin *Corynebacterium diphtheriae* thioether with human beta-amyloid protein 42-(1-7)-peptidylcysteine

²⁴ INN selected before the implementation of the *ef*- suffix.

²⁵ The names and the descriptions of toxins are published in Annex 4.1 of "International Nonproprietary Names (INN) for pharmaceutical substances. Names for radicals, groups & others: comprehensive list (WHO/EMP/RHT/TSN/2015.1)".

-motide

amilomotide (105)

virus like particle of bacteriophage Q-beta coat protein that is coupled to multiple copies of human beta-amyloid1-6 peptide fragment;
reaction products of bacteriophage Q-beta coat protein with human beta-amyloid protein-(1-6)-peptidylglycylglycyl-L-cysteine and 3-(2,5-dioxo-2,5-dihydro-1*H*-pyrrole-1-yl)-*N*-{(2,5-dioxopyrrolidin-1-yl)oxy}-6-oxohexyl}propanamide

sultimotide alfa (117)

a fusion protein consisting of fragments of hepatitis B virus transcription factor X, large S-protein antigen (envelope antigen), B antigen (core antigen) and of a C-terminal six-histidine tag, expressed by engineered whole heat-killed *Saccharomyces cerevisiae*, glycoform alfa;
Met-Ala-Asp-Glu-Ala-Pro-Thr-Ser-{des-(69-83)-[P⁵⁹>F]protein X (hepatitis B virus)-(52-127)-peptide (9-69)}-
{[M¹>E,G³>Q,Q¹⁰>K,P¹⁹S,G³⁵>R,N³⁹>A,H⁵¹>T,P⁶⁵>L,T⁸⁶>Q,A⁹¹>N]large S protein (hepatitis B virus) (70-243)}- {[T⁴>I,V²⁵>I,N²⁰⁷>S,L²⁰⁹>V,L²¹³>I]small S protein (hepatitis B virus) (244-469)}- {des-Met¹-[S¹²>T]capsid protein (hepatitis B virus) (470-651)}-His₆ (652-657) fusion protein, produced in *Saccharomyces cerevisiae*, glycoform alfa

tecemotide (108)

human mucin-1 (carcinoma-associated mucin, episialin, CD227)-(107-131)-peptide (sequence 40 times repeated) fusion protein with 6-*N*-hexadecanoyl-L-lysylglycine

zastumotide (110)

19,137,308,342,395-penta[S-(2-amino-2-oxoethyl)]-[2-aspartic acid(K²>D),3-proline(L³>P)]glycerophosphoryl diester phosphodiesterase (*Haemophilus influenzae* strain 86-028NP EC 3.1.4.46)-(1-127)-peptide fusion protein with [2-aspartic acid(P²>D)]human melanoma-associated antigen 3 (MAGE-3 antigen, antigen MZ2-D, cancer/testis antigen 1.3 or CT1.3) fusion protein with diglycylheptahistidine}

-cog

efmorotocog alfa (111)

recombinant DNA derived (1-742)-(1637-2332)-human blood coagulation factor VIII fusion protein with immunoglobulin G1 Fc domain fragment, produced in HEK293H cells, glycoform alfa:
des-(743-1636)-human blood coagulation factor VIII (antihemophilic factor, procoagulant component) fusion protein with human immunoglobulin G1 Fc fragment (IGHG1*01 H-CH2-CH3)-(6-231)-peptide (1444-6':1447-9')-bisdisulfide with human immunoglobulin G1 Fc fragment (IGHG1*01 H-CH2-CH3)-(6-231)-peptide

eftrenonacog alfa (109)

recombinant DNA derived human blood coagulation factor IX fusion protein with one Fc fragment of the human immunoglobulin G1 Fc fragment dimer, produced in HEK293H cells (glycoform alfa):
human blood coagulation factor IX (EC 3.4.21.22, Christmas factor, plasma thromboplastin component) variant 148-T, fusion protein with human immunoglobulin G1 Fc fragment (IGHG1*01 H-CH2-CH3)-(6-231)-peptide (421-6':424-9')-bisdisulfide with human immunoglobulin G1 Fc fragment (IGHG1*01 H-CH2-CH3)-(6-231)-peptide

-stim

eflapegrastim (112)

human granulocyte colony-stimulating factor and human IgG4 Fc dimer linked together with polyethylene glycol derivative, produced in *Escherichia coli*:

$N^{\alpha,1},N^{1,9'}$ -[ω -(oxypropane-1,3-diyl)- α -(propane-1,3-diyl)poly(oxyethylene)] des-(1-l-alanine,37-39)-[18-l-serine(C>S),69-l-serine(P>S)]human granulocyte colony-stimulating factor (G-CSF, pluripoietin) (1-174)-peptide and des-(1-8)-human immunoglobulin G4 Fc fragment (IGHG4*01 H-CH2-CH3) (9'-229')-peptide dimer (11'-11'')-disulfide

romiplostim (97)²⁶

L-methionyl[human immunoglobulin heavy constant gamma 1-(227 C-terminal residues)-peptide (Fc fragment)] fusion protein with 41 amino acids peptide, (7-7':10,10')-bisdisulfide dimer

Others:

blisibimod (107)²⁶

B-cell activating factor (BAFF)-binding peptide fragment/human IgG1 Fc fusion protein

dianexin (109)

recombinant DNA derived annexin A5 dimer covalently linked by a 14 residues peptide linker, produced in *Escherichia coli* (nonglycosylated):

L-methionyl-human annexin A5 fusion protein with glycyl-L-seryl-L-leucyl-L- α -glutamyl-L-valyl-L-leucyl-L-phenylalanyl-L-glutaminyglycyl-L-prolyl-L-serylglycyl-L-lysyl-L-leucyl-human annexin A5

efaprinermin alfa (120)

tumor necrosis factor ligand superfamily protein TNFSF18 (human) extracellular (71-199)-peptide trimer [three fused copies (1-129, 130-258, 259-387)] fusion protein with immunoglobulin G1 (human) Fc fragment (227 C-terminal residues) (388-614), natural [D⁵²³>E,L⁵²⁵>M] variant [*Homo sapiens* IGHG1*03, hinge (388-397), CH2 (398-507), CH3 (508-612), CHS (613-614)], (393-393',396-396')-bisdisulfide dimer, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

efepoetin alfa (117)

human erythropoietin (epoetin alfa) fused to a hybrid human immunoglobulin (Ig), consisting of the Fc fragment of the IgG4 fused to the hinge and amino-terminus of the IgD heavy chain isotype 2, produced in Chinese hamster ovary (CHO) cells, glycoform alfa; [human erythropoietin (EPO) (1-166)]-[immunoglobulin heavy chain delta (IGHD) isoform 2 constant region (133-170)-peptide (C-terminal hinge region and N-terminal CH2 domain) (167-204)]-[immunoglobulin heavy chain gamma 4 (IGHG4) constant region (121-327)-peptide (CH2 and CH3 domains) (205-411)]-fusion protein, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

efgivanermin (120)

immunoglobulin γ 1 chain Fc fragment [*Homo sapiens* IGHG1*03 {hinge 1,4-del, C⁵>L(1), CH2 (12-121), CH3 (122-226), CHS (227-228)}-(1-228)] fusion protein with pentakis(tetraglycyl-l-seryl)[*Homo sapiens* coronin-1A precursor (tryptophan aspartate-containing coat protein, TACO) fragment 430-461 (254-285)]-(229-285) fusion protein with tetraglycyl[*Homo sapiens* tumor necrosis factor ligand superfamily member 18 (glucocorticoid-induced TNF-related ligand) [183-Asn(D>N)]precursor fragment 72-199 (289-417)]-(286-417); hexamer stabilized with hexakisdisulfide bridges between 12 cysteines at position 7 and 10; produced in Chinese hamster ovary (CHO) cells, glycoform alfa

²⁶ INN selected before the implementation of the *ef*- suffix.

eflenograstim alfa (117)

human granulocyte-colony stimulating factor (G-CSF) fused to a hybrid human immunoglobulin consisting of the Fc fragment of the IgG4 fused to the hinge region and amino-terminus of the IgD heavy chain isotype 2, produced in Chinese hamster ovary (CHO) cells, glycoform alfa;

[human granulocyte-colony stimulating factor (G-CSF) short isoform (1-174)]-[immunoglobulin heavy chain delta (IGHD) constant region isoform 2 (133-170)-peptide (C-terminal hinge and N-terminal CH2 domains) (175-212)]-[immunoglobulin heavy chain gamma 4 (IGHG4) constant region (121-327)-peptide (CH2 and CH3 domains) (213-419)]-fusion protein, (203-203')-disulfide dimer, produced in Chinese hamster ovary (CHO) cells, glycoform alfa

isunakinra (113)

human interleukin-1 beta-(1-8)-peptide fusion protein with human interleukin-1 receptor antagonist protein-(14-45)-peptide fusion protein with human interleukin-1 beta-(42-120)-peptide fusion protein with human interleukin-1 receptor antagonist protein-(120-147)-peptide fusion protein with human interleukin-1 beta-(148-153)-peptide non-glycosylated

somavaratan (112)

rDNA derived human somatropin (growth hormone of 191 residues) fusion protein with a hydrophilic amino acid sequence* (913 residues) at the N-terminus and another** (146 residues) at the C-terminus, produced in *Escherichia coli*.

* starting with alanine plus 76 dodecapeptides: EPAGSPTSTEEG (AE3G2P2S2T2), three different sequences of AG3P2S4T2 and 72 of 4 different sequences of AE2G2P2S3T2

** starting with glycyglycine plus 12 dodecapeptides of 4 different sequences of AE2G2P2S3T2

tengonermin (118)

human tumor necrosis factor (7-163) fused at the N-terminus to a peptide (1-6) ligand of the human CD13 antigen, trimer, produced in *Escherichia coli*;

l-cysteinyl-l-asparaginylglycyl-l-arginyl-l-cysteinylglycyl (1-6, CNGRCG, ligand of the human CD13 antigen)-human tumor necrosis factor soluble form (7-163), non-covalent trimer, produced in *Escherichia coli*

topsalsyn (111)

recombinant DNA derived proaerolysin, pore-forming protein, from *Aeromonas hydrophila*, with the furin site substituted with a prostate specific antigen (PSA) cleavage site, fusion protein with 6 histidines, produced in *Escherichia coli* (nonglycosylated):

[427-L-histidine(K>H),428-L-serine(V>S),429-L-serine(R>S),430-L-lysine(R>K),431-L-leucine(A>L),432-L-glutamine(R>Q)]proaerolysin *Aeromonas hydrophila* fusion protein with hexa-L-histidine

torapsel (91)²⁷

42-89-glycoprotein (human clone PMT21:PL85 P-selectin glycoprotein ligand fusion protein with immunoglobulin (human constant region)

trebananib (106)²⁷

immunoglobulin G1 Fc fragment fused with two synthetic polypeptides that bind the *Homo sapiens* ANGPT2 (angiopoietin 2);

methionyl (1) -gamma1 heavy chain fragment (2-228) [*Homo sapiens* IGHG1*01 hinge (EPKSC 1-5>del) (2-11), CH2 (12-121), CH3 (122-228)] fused, at the C-terminal end, with a synthetic polypeptide that comprises two 14-mer amino acid repeats that bind angiopoietin 2 (229-287) [linker (229-235) -14-mer (236-249) -linker (250-271) -14-mer (272-285) -leucyl-glutamate]; (7-7':10-10')-bisdisulfide dimer

²⁷ INN selected before the implementation of the *ef*- suffix.

verpasep caltespen (95)

60 kDa chaperonin 2 (heat shock protein 65 from *Mycobacterium bovis* strain BCG) (*caltespen*)
fusion protein with L-histidylprotein E7 from human papillomavirus type 16 (*verpasep*).

ANNEX 2.

List of INN for conjugated proteins²⁸

classified by groups

-ase

bovhyaluronidase azoximer (112)

hyaluronidase-2 bovine (hyaluronoglucosaminidase-2, Hyal-2, EC 3.2.1.35) *Bos taurus*
precursor protein linked to poly[[1-(carboxymethyl)piperazin-1-ium-1,4-diyl
bromide]ethylene-co-[(piperazine-1,4-diyl-1-oxide)ethylene]] by an amido covalent bond

-tide

tozuleristide (115)

$N^{6,27}$ -[6-(2-[(1*E*,2*E*,4*E*,6*E*)-7-[1,1-dimethyl-3-(4-sulfonatobutyl)-1*H*-benzo[*e*]indol-3-ium-2-yl]hepta-2,4,6-trien-1-ylidene)-1,1-dimethyl-1,2-dihydro-3*H*-benzo[*e*]indol-3-yl]hexanoyl)-
[Lys¹⁵>Arg,Lys²³>Arg]chlorotoxin (*Leiurus quinquestriatus quinquestriatus*) (Egyptian scorpion)

-tide & -xetan (for chelating agents)

satoreotide trizoxetan (114)

S^2,S^7 -cyclo[*N*-{(4*RS*)-4-[4,7-bis(carboxymethyl)-1,4,7-triazonan-1-yl]-4-carboxybutanoyl}-4-chloro-L-phenylalanyl-D-cysteiny-4-[(4*S*)-2,6-dioxo-1,3-diazinane-4-carboxamido]-L-phenylalanyl-4-(carbamoylamino)-D-phenylalanyl-L-lysyl-L-threonyl-L-cysteiny-4-D-tyrosinamide]

trizoxetan

(4*RS*)-4-[4,7-bis(carboxymethyl)-1,4,7-triazonan-1-yl]-4-carboxybutanoyl

satoreotide tetraxetan (118)

S^2,S^7 -cyclo[4-chloro-*N*-{[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecan-1-yl]acetyl}-1-phenylalanyl-D-cysteiny-4-[(4*S*)-2,6-dioxo-1,3-diazinane-4-carboxamido]-1-phenylalanyl-4-(carbamoylamino)-D-phenylalanyl-L-lysyl-L-threonyl-L-cysteiny-4-D-tyrosinamide]

vipivotide tetraxetan (120)

N-[(N^6 -{3-(naphthalen-2-yl)-*N*-[*trans*-4-({2-[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecan-1-yl]acetamido}methyl)cyclohexane-1-carbonyl]-1-alanyl}-1-lysyl- N^2 -yl)carbonyl]-1-glutamic acid

-mab

tamrintamab pamozirine (120)

immunoglobulin G1-kappa, anti-[*Homo sapiens* DPEP3 (dipeptidase 3)], humanized monoclonal antibody conjugated to a pyrrolbenzodiazepine dimer (PBD) SC-DR002 via light Cys215;
gamma1 heavy chain humanized (1-452) [VH (*Homo sapiens* IGHV1-69*01 (85.7%) -(IGHD)-IGHJ6*01 (90.9%)) [8.8.16] (1-123) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 K120 (220)

²⁸ Two or more entities that are linked together by a chemical reaction *in vitro* after they have been separately produced.

(124-221), hinge C5>S (226) (222-236), CH2 (237-346), CH3 D12 (362), L14 (364) (347-451), CHS K>del (452) (124-452)], non-covalently associated with kappa light chain humanized (1'-215') [V-KAPPA (*Homo sapiens* IGKV3D-20*01 (86.50%) -IGKJ2*01 (100.0%)) [7.3.9] (1'-108'),-*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (154), V101 (192) (109'-215')]; dimer (232-232":235-235")-bisdisulfide; conjugated at each CL C126 (215', 215'") to a pyrrolbenzodiazepine dimer (PBD) SC-DR002 via a protease-cleavable maleimide linker (LD6.23)

pamozirine

(111aS,911S,911aS,16S,19S,273RS)-911-hydroxy-17,97-dimethoxy-12,92,16-trimethyl-15,95-10,15,18,21,272,275-octa-19-(propan-2-yl)-15,111a,911,911a-tetrahydro-11H,91H,95H-2,8,11-trioxa-14,17,20-triaza-1(8),9(8,10)-bis(pyrrolo[1,2-c][1,4]benzodiazepina)-27-(1)-pyrrolidina-13(1,4)-benzenaheptacosaphan-273-yle

trastuzumab duocarmazine (115)

immunoglobulin G1-kappa, anti-[*Homo sapiens* ERBB2 (epidermal growth factor receptor 2, receptor tyrosine-protein kinase erbB-2, EGFR2, HER2, HER-2, p185c-erbB2, NEU, CD340)], humanized monoclonal antibody conjugated to the pro-drug *seco*-duocarmycin-hydroxybenzamide-azaindole (*seco*-DUBA);

gamma1 heavy chain (1-449) [humanized VH (*Homo sapiens* (IGHV3-66-*01 (81.60%) - (IGHD)-IGHJ6*01) [8.8.13] (1-120) -*Homo sapiens* IGHG1*01, G1m17, nG1m1 (CH1 (121-218), hinge (219-233), CH2 (234-343), CH3 D12>E (359), L14>M (361) (344-448), CHS K>del (449)) (121-449)], (223-214')-disulfide with kappa light chain (1'-214') [humanized V-KAPPA (*Homo sapiens* IGKV1-39*01 (86.30%) -IGKJ1*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimer (229-229":232-232")-bisdisulfide, conjugated on an average of 2 or 4 cysteines, to *seco*-DUBA via the cleavable linker *N*-[2-(2-maleimidoethoxy)ethoxycarbonyl]-L-valyl-L-citrullinyl-*p*-aminobenzyloxycarbonyl-*N*-[2-(2-hydroxyethoxy)ethyl]-*N*-[2-(methylamino)ethyl]carbamoyl

duocarmazine

(6¹S,19S,22S,31³RS)-19-[3-(carbamoylamino)propyl]-6¹-(chloromethyl)-1⁴-hydroxy-9-[2-(2-hydroxyethoxy)ethyl]-6⁹,12-dimethyl-2,5,8,13,18,21,24,31²,31⁵-nona-22-(propan-2-yl)-6¹,6²-dihydro-7,14,25,28-tetraoxa-3,9,12,17,20,23-hexaaza-6(3,5)-benzo[*e*]indola-4(6,2)-imidazo[1,2-*a*]pyridina-31(1)-pyrrolidina-1(1),16(1,4)-dibenzenahentriacontaphan-31³-yl

-*ma*b & *biotin*

iodine (¹³¹I) derlotuximab biotin (113)

immunoglobulin G1-kappa, anti-[*Homo sapiens* DNA/histone 1 (H1) complex], chimeric monoclonal antibody radiolabeled with iodine-131 and biotinylated; gamma1 heavy chain (1-450) [*Mus musculus* VH (IGHV2-6-5*01 - (IGHD)-IGHJ4*01) [8.7.14] (1-120) - *Homo sapiens* IGHG1*01, G1m17,1 (CH1 V121>A (218) (121-218), hinge (219-233), CH2 (234-343), CH3 (344-448), CHS (449-450)) (121-450)], (223-215')-disulfide with kappa light chain (1'-215') [*Mus musculus* V-KAPPA (IGKV4-57-1*01 -IGKJ1*01) [7.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (109'-215')]; dimer (229-229":232-232")-bisdisulfide; (¹³¹I) iodinated with iodine-131 covalently linked to tyrosines, and biotinylated

*biotin (RL45)*²⁹

5-[(3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-*d*]imidazol-4-yl]pentanoic acid

²⁹ Recommended list number.

-mab & -dotin³⁰ (for synthetic derivatives of dolastatin series)

lupartumab amadotin (115)

immunoglobulin G1-lambda1, anti-[*Homo sapiens* LYPD3 (Ly6/PLAUR domain containing 3, GPI-anchored cell-surface protein C4.4a, C4.4A)], *Homo sapiens* monoclonal antibody conjugated to an auristatin W derivative;

gamma1 heavy chain (1-446) [*Homo sapiens* VH (IGHV3-48*03 (92.90%) -(IGHD) - IGHJ4*01) [8.8.10](1-117) -IGHG1*01, Gm17,1 (CH1 (118-215), hinge (216-230), CH2 (231-340), CH3 (341-445), CHS K>del (446)) (118-446)], (220-216')-disulfide with lambda1 light chain (1'-217') [*Homo sapiens* V-LAMBDA (IGLV1-47*01 (87.90%) -IGLJ2*01) [9.3.11] (1'-111') -IGLC2*01 (112'-217')]; dimer (226-226":229-229")-bisdisulfide; S-substituted on an average of 4 reduced cysteinyl by reaction with *N*-demethyl-*N*-[4-(6-maleimidohexanohydrazido)-4-oxobutyl]auristatin W amide

amadotin

(3*RS*)-1-[(3*R*,4*S*,7*S*,10*S*)-1-[(2*S*)-2-[(1*R*,2*R*)-3-[(2*S*)-1-amino-3-(1*H*-indol-3-yl)-1-oxopropan-2-yl]amino]-1-methoxy-2-methyl-3-oxopropyl]pyrrolidin-1-yl]-4-[(2*S*)-butan-2-yl]-3-methoxy-5,11-dimethyl-1,6,9,15,18-pentaoxo-7,10-di(propan-2-yl)-5,8,11,16,17-pentaazatricosan-23-yl]-2,5-dioxopyrrolidin-3-yl

aprutumab ixadotin (115)

immunoglobulin G1-lambda1, anti-[*Homo sapiens* FGFR2 (fibroblast growth factor receptor 2, keratinocyte growth factor receptor, KGFR, CD332)], *Homo sapiens* monoclonal antibody conjugated to an auristatin W derivative;

gamma1 heavy chain (1-451) [*Homo sapiens* VH (IGHV3-23*01 (98.00%) -(IGHD) - IGHJ5*02) [8.8.15](1-122) -IGHG1*01, Gm17,1 (CH1 (123-220), hinge (221-235), CH2 (236-345), CH3 (346-450), CHS K>del (451)) (123-451)], (225-215')-disulfide with lambda1 light chain (1'-216') [*Homo sapiens* V-LAMBDA (IGLV1-47*01 (90.70%) -IGLJ3*02) [8.3.11] (1'-110') -IGLC2*01 (111'-216')]; dimer (231-231":234-234")-bisdisulfide; conjugated, on an average of 4 lysyl, to *N*-(5-carboxypentyl)-*N*-demethyl-auristatin W (AW) C^{1.5}-(1,2-oxazinan-2-yl) derivative

ixadotin

6-[(2-{*N*-methyl-L-valyl-L-valyl-(3*R*,4*S*,5*S*)-3-methoxy-5-methyl-4-(methylamino)heptanoyl-(2*R*,3*R*)-3-methoxy-2-methyl-3-[(2*S*)-pyrrolidin-2-yl]propanoyl-L-tryptophyl}-1,2-oxazinan)-*N*^{2.1}-yl]hexanoyl

belantamab mafodotin (118)

immunoglobulin G1-kappa, anti-[*Homo sapiens* TNFRSF17 (TNF receptor superfamily member 17, tumor necrosis factor receptor superfamily, member 17, B cell maturation antigen, BCMA, BCM, TNFRSF13A, CD269)], humanized monoclonal antibody conjugated to auristatin F;

gamma1 heavy chain (1-451) [humanized VH (*Homo sapiens* IGHV1-69*06 (83.7%) -(IGHD)- IGHJ4*01 (85.7%)) [8.8.14] (1-121) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 K120 (218) (122-219), hinge (220-234), CH2 (235-344), CH3 D12 (360), L14 (362) (345-449), CHS (450-451)) (122-451)], (224-214')-disulfide with kappa light chain (1'-214') [humanized V-KAPPA (*Homo sapiens* IGKV1-33*01 (90.5%) -IGKJ2*02 (100%)) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 A45.1 (153), V101 (191)(108'-214')]; dimer (230-230":233-233")-bisdisulfide; conjugated, on an average of 4 cysteinyl, to monomethylauristatin F (MMAF), via a noncleavable maleimidocaproyl (mc) linker

³⁰ The names ending in *-dotin* and the descriptions are published in Annex 4.2 of "International Nonproprietary Names (INN) for pharmaceutical substances. Names for radicals, groups & others: comprehensive list (WHO/EMP/RHT/TSN/2015.1)".

denintuzumab mafodotin (111)

immunoglobulin G1-kappa auristatin F conjugate, anti-[*Homo sapiens* CD19 (B lymphocyte surface antigen B4, Leu-12)], humanized monoclonal antibody;
gamma1 heavy chain (1-450) [humanized VH (*Homo sapiens* IGHV4-31*02 (84.80%) - (IGHD)-IGHJ4*01) [10.7.12] (1-120) -*Homo sapiens* IGHG1*01 (CH1 (121-218), hinge (219-233), CH2 (234-343), CH3 (344-448), CHS (449-450)) (121-450)], (223-213')-disulfide with kappa light chain (1'-213') [humanized V-KAPPA (*Homo sapiens* IGKV3-11*01 (85.30%) - IGKJ2*02) [5.3.9] (1'-106') -*Homo sapiens* IGKC*01 (107'-213')]; dimer (229-229":232-232")-bisdisulfide; conjugated, on an average of 4 cysteinyl, to monomethylauristatin F (MMAF), via a noncleavable maleimidocaproyl (mc) linker

depatuxizumab mafodotin (115)

immunoglobulin G1-kappa, anti-[*Homo sapiens* EGFR (epidermal growth factor receptor, receptor tyrosine-protein kinase erbB-1, ERBB1, HER1, HER-1, ERBB)], humanized and chimeric monoclonal antibody conjugated to auristatin F;
gamma1 heavy chain humanized (1-446) [humanized VH (*Homo sapiens* IGHV4-30-4*01 (84.50%) - (IGHD)-IGHJ4*01) [9.7.9] (1-116) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (117-214), hinge (215-229), CH2 (230-339), CH3 (340-444), CHS (445-446)) (117-446)], (219-214')-disulfide with kappa light chain chimeric (1'-214') [*Mus musculus* V-KAPPA (*Mus musculus* IGKV14-100*01 -IGKJ1*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimer (225-225":228-228")-bisdisulfide; conjugated, on an average of 4 cysteinyl, to monomethylauristatin F (MMAF), via a noncleavable maleimidocaproyl (mc) linker

vorsetuzumab mafodotin (107)

immunoglobulin G1-kappa auristatin F conjugate, anti-[*Homo sapiens* CD70 (tumor necrosis factor superfamily member 7, TNFSF7, CD27LG, CD27L)], humanized monoclonal antibody conjugated to auristatin F;
gamma1 heavy chain (1-448) [humanized VH (*Homo sapiens* IGHV1-2*02 (86.70%) - (IGHD)-IGHJ6*01) [8.8.11] (1-118) -*Homo sapiens* IGHG1*01 (119-448)], (221-218')-disulfide (if not conjugated) with kappa light chain (1'-218') [humanized V-KAPPA (*Homo sapiens* IGKV4-1*01 (79.20%) -IGKJ1*01) [10.3.9] (1'-111') -*Homo sapiens* IGKC*01 (112'-218')]; (227-227":230-230")-bisdisulfide dimer; conjugated, on an average of 3 to 5 cysteinyl, to monomethylauristatin F (MMAF), via a non-cleavable maleimidocaproyl (mc) linker

cofetuzumab pelidotin (117)

immunoglobulin G1-kappa, anti-[*Homo sapiens* PTK7 (protein tyrosine kinase 7, colon carcinoma kinase 4, CCK4) extracellular domain], humanized monoclonal antibody, conjugated to auristatin-0101;
gamma1 heavy chain (1-448) [humanized VH (*Homo sapiens* IGHV1-3*01 (81.60%) - (IGHD)-IGHJ4*01) [8.8.12] (1-119) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 K120 (216) (120-217), hinge (218-232), CH2 (233-342), CH3 D12 (358), L14 (360) (343-447), CHS K>del (448)) (120-448)], (222-218')-disulfide with kappa light chain (1'-218') [humanized V-KAPPA (*Homo sapiens* IGKV3-11*01 (83.80%) -IGKJ4*01) [10.3.9] (1'-111') -*Homo sapiens* IGKC*01, Km3 A45.1 (157), V101 (195) (112'-218')]; dimer (228-228":231-231")-bisdisulfide; conjugated, on an average of 4 cysteinyl, to auristatin-0101 (Aur0101), via a cleavable maleimidocaproyl-valyl-citrullinyl-*p*-aminobenzyloxycarbonyl (mc-val-cit-PABC) type linker

pelidotin

(3*RS*)-1-(6-({[(2*S*)-1-({[(2*S*)-5-(carbamoylamino)-1-[4-({[(1-({[(2*S*)-1-({[(3*R*,4*S*,5*S*)-3-methoxy-1-({(2*S*)-2-[(1*R*,2*R*)-1-methoxy-2-methyl-3-oxo-3-{{[(1*S*)-2-phenyl-1-(1,3-thiazol-2-yl)ethyl]amino}propyl]pyrrolidin-1-yl]-5-methyl-1-oxoheptan-4-yl](methyl)amino}-3-methyl-1-oxobutan-2-yl]amino}-2-methyl-1-oxopropan-2-yl)carbamoyl]oxy}methyl]anilino)-1-oxopentan-2-yl]amino)-3-methyl-1-oxobutan-2-yl]amino}-6-oxohexyl)-2,5-dioxopyrrolidin-3-yl

azintuxizumab vedotin (116)

immunoglobulin G1-kappa, anti-[*Homo sapiens* SLAMF7 (SLAM family member 7, CD2 subset 1, CS1, CD2-like receptor-activating cytotoxic cells, CRACC, 19A24, CD319)], humanized and chimeric monoclonal antibody conjugated to auristatin E; gamma1 heavy chain (1-447) [humanized VH (*Homo sapiens* IGHV3-7*01(91.80%) -(IGHD) -IGHJ4*01 L123>T (112)) [8.8.10] (1-117) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 R120>K (214) (118-215), hinge (216-230), CH2 (231-340), CH3 E12(366), M14 (368) (341-445), CHS (446-447) (118-447)], (220-220')- disulfide with kappa light chain chimeric (1'-220') [*Mus musculus* V-KAPPA (IGKV1-110*01 (93.00%) -IGKJ4*01) [11.3.10] (1'-113') -*Homo sapiens* IGKC*01, Km3 A45.1 (159), V101 (197) (114'-220')]; dimer (226-226":229-229")-bisdisulfide; conjugated, on an average of 3 cysteinyl, to monomethylauristatin E (MMAE), via a cleavable maleimidocaproyl-valyl-citrullinyl-*p*-aminobenzyloxycarbonyl (mc-val-cit-PABC) type linker.

brentuximab vedotin (103)

immunoglobulin G1-kappa auristatin E conjugate, anti-[*Homo sapiens* TNFRSF8 (tumor necrosis factor receptor superfamily member 8, KI-1, CD30)], chimeric monoclonal antibody conjugated to auristatin E; gamma1 heavy chain (1-446) [*Mus musculus* VH (IGHV1-84*02 -(IGHD)-IGHJ3*01) [8.8.10] (1-117) -*Homo sapiens* IGHG1*01 CH3 K130>del (118-446)], (220-218')-disulfide (if not conjugated) with kappa light chain (1'-218') [*Mus musculus* V-KAPPA (IGKV3-4*01 -IGKJ1*01) [10.3.9] (1'-111') -*Homo sapiens* IGKC*01 (112'-218')];(226-226")-disulfide dimer; conjugated, on an average of 3 to 5 cysteinyl, to monomethylauristatin E (MMAE), via a maleimidocaproyl-valyl-citrullinyl-*p*-aminobenzyloxycarbonyl (mc-val-cit-PABC) linker

disitamab vedotin (120)

immunoglobulin G1-kappa, anti-[*Homo sapiens* ERBB2 (epidermal growth factor receptor 2, receptor tyrosine-protein kinase erbB-2, EGFR2, HER2, HER-2, p185c-erbB2, NEU, CD340)], humanized monoclonal antibody conjugated to auristatin E; gamma1 heavy chain humanized (1-445) [VH (*Homo sapiens* IGHV1-69-2*01 (83.5%) - (IGHD) -IGHJ1*01 (92.9%)) [8.8.8] (1-115) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 R120>K (212) (116-213), hinge (214-228), CH2 (229-338), CH3 E12 (354), M14 (357) (339-443), CHS (444-445)) (116-445)] (218-212')-disulfide with kappa light chain humanized (1'-212') [V-KAPPA (*Homo sapiens* IGKV1-39*01 (83.3%) -IGKJ4*01 (100%)) [6.3.7] (1'-105') -*Homo sapiens* IGKC*01 (100%) Km3 A45.1 (151), V101 (189) (106'-212')]; dimer (224-224":227-227")-bisdisulfide; conjugated on an average of 4 cysteinyl to monomethylauristatin E (MMAE), via a cleavable maleimidocaproyl-valyl-citrullinyl-*p*-aminobenzyloxycarbonyl (mc-val-cit-PABC) type linker

enapotamab vedotin (118)

immunoglobulin G1-kappa, anti-[*Homo sapiens* AXL (AXL receptor tyrosine kinase, tyrosine-protein kinase receptor UFO)], *Homo sapiens* monoclonal antibody conjugated to auristatin E; gamma1 heavy chain (1-445) [*Homo sapiens* VH (IGHV3-23*01 (95.9%) -(IGHD) -IGHJ3*02 (100%)) [8.8.9] (1-116) -*Homo sapiens* IGHG1*03, G1m3 nG1m1 (CH1 R120 (213) (117-214), hinge (215-229), CH2 (230-339), CH3 E12 (355), M14 (357) (340-444), CHS K>del (445)) (117-445)], (219-215')-disulfide with kappa light chain (1'-215') [*Homo sapiens* V-KAPPA (IGKV3-20*01 (100%) -IGKJ2*01 (100%)) [7.3.9] (1'-108') -*Homo sapiens* IGKC*01, Km3 A45.1 (154), V101 (192) (109'-215')]; dimer (225-225":228-228")-bisdisulfide; conjugated, on an average of 4 cysteinyl, to monomethylauristatin E (MMAE), via a cleavable maleimidocaproyl-valyl-citrullinyl-*p*-aminobenzyloxycarbonyl (mc-val-cit-PABC) type linker

enfortumab vedotin (109)

immunoglobulin G1-kappa, anti-[*Homo sapiens* PVRL4 (poliovirus receptor-related 4, nectin-4, nectin 4, PPR4, LNIR), *Homo sapiens* monoclonal antibody conjugated to auristatin E; gamma1 heavy chain (1-447) [*Homo sapiens* VH (IGHV3-48*02 (98.00%) -(IGHD)-IGHJ6*01) [8.8.10] (1-117) -IGHG1*03 (CH1 (118-215), hinge (216-230), CH2 (231-340), CH3 (341-445), CHS (446-447)) (118-447)], (220-214')-disulfide with kappa light chain (1'-214') [*Homo sapiens* V-KAPPA (IGKV1-12*01 (96.80%) -IGKJ4*01) [6.3.9] (1'-107') -IGKC*01 (108'-214')]; dimer (226-226":229-229")-bisdisulfide; conjugated, on an average of 3 to 4 cysteinyl, to monomethylauristatin E (MMAE), via a cleavable maleimidocaproyl-valyl-citrullinyl-*p*-aminobenzylcarbamate (mc-val-cit-PABC) linker

glembatumumab vedotin (113)

immunoglobulin G2-kappa, anti-[*Homo sapiens* GPNMB (glycoprotein (transmembrane) nmb, glycoprotein transmembrane NMB, glycoprotein nonmetastatic melanoma protein B, CG56972, osteoactivin, hematopoietic growth factor inducible neurokinin-1 type, HGFIN) extracellular domain], *Homo sapiens* monoclonal antibody conjugated to auristatin E; gamma2 heavy chain (1-445) [*Homo sapiens* VH (IGHV4-31*02 (94.90%) -(IGHD)-IGHJ4*01) [10.7.11] (1-119) -IGHG2*01, G2m.. (CH1 (120-217), hinge (218-229), CH2 (230-338), CH3 (339-443), CHS (444-445)) (120-445)], (133-215')-disulfide with kappa light chain (1'-215') [*Homo sapiens* V-KAPPA (IGKV3-15*01 (96.80%) -IGKJ1*01) [6.3.10] (1'-108') -IGKC*01, Km3 (109'-215')]; dimer (221-221":222-222":225-225":228-228")-tetrakisdisulfide; conjugated, on an average of 5 cysteinyl, to monomethylauristatin E (MMAE), via a cleavable maleimidocaproyl-valyl-citrullinyl-*p*-aminobenzylloxycarbonyl (mc-val-cit-PABC) type linker

iladatuzumab vedotin (117)

immunoglobulin G1-kappa, anti-[*Homo sapiens*CD79B (immunoglobulin-associated CD79 beta)], humanized monoclonal antibody conjugated to auristatin E; gamma1 heavy chain (1-447) [humanized VH (*Homo sapiens* IGHV3-23*04 (76.50%) -(IGHD)-IGHJ4*01) [8.8.10] (1-117) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 A1.4>C (118), R120>K (214) (118-215), hinge (216-230), CH2 (231-340), CH3 E12 (356), M14 (358) (341-445), CHS (446-447)) (119-447)], (220-218')-disulfide with kappa light chain (1'-218') [humanized V-KAPPA (*Homo sapiens* IGKV1-39*01 (85.90%) -IGKJ1*01) [10.3.9] (1'-111') -*Homo sapiens* IGKC*01, Km3 A45.1 (157), V101 (195) (112'-218')]; dimer (226-226":229-229")-bisdisulfide; conjugated on 2 cysteinyl (at the position gamma1 CH1 1.4 (118, 118")), to monomethylauristatin E (MMAE), via a cleavable maleimidocaproyl-valyl-citrullinyl-*p*-aminobenzylloxycarbonyl (mc-val-cit-PABC) type linker

indusatumab vedotin (112)

immunoglobulin G1-kappa, anti-[*Homo sapiens* GUCY2C (guanylate cyclase 2C, guanylyl cyclase C, GCC, guanylate cyclase C, GC-C, heat-stable enterotoxin receptor, hSTAR, intestinal guanylate cyclase)], *Homo sapiens* monoclonal antibody; gamma1 heavy chain (1-449) [*Homo sapiens* VH (IGHV4-34*01 (94.80%) -(IGHD)-IGHJ1*01) [8.7.13] (1-119)-IGHG1*01 (CH1 (120-217), hinge (218-232), CH2 (233-342), CH3 (343-447), CHS (448-449)) (120-449)], (222-214')-disulfide with kappa light chain (1'-214') [*Homo sapiens* V-KAPPA (IGKV3-15*01 (95.80%) -IGKJ1*01 K123>N (103) [6.3.9] (1'-107') -IGKC*01 (108'-214')]; dimer (228-228":231-231")-bisdisulfide; conjugated, on an average of 3 to 4 cysteinyl, to monomethylauristatin E (MMAE), via a cleavable maleimidocaproyl-valyl-citrullinyl-*p*-aminobenzylloxycarbonyl (mc-val-cit-PABC) type linker

ladiratuzumab vedotin (117)

immunoglobulin G1-kappa, anti-[*Homo sapiens* SLC39A6 (solute carrier family 39 member 6, solute carrier family 39 (metal ion transporter) member 6, solute carrier family 39 (zinc transporter) member 6, LIV-1)], humanized monoclonal antibody conjugated to auristatin E; gamma1 heavy chain (1-450) [humanized VH (*Homo sapiens* IGHV1-2*02 (87.60%) -(IGHD)-IGHJ4*01) [8.8.13] (1-120) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 K120 (217) (121-218), hinge (219-233), CH2 (234-343), CH3 D12 (359), L14 (361) (344-448), CHS (449-450)) (121-450)], (223-219')-disulfide with kappa light chain (1'-219') [humanized V-KAPPA (*Homo sapiens* IGKV2-30*02 (89.00%) -IGKJ4*01) [11.3.9] (1'-112') -*Homo sapiens* IGKC*01, Km3 A45.1 (158), V101 (196) (113'-219')]; dimer (229-229":232-232")-bisdisulfide; conjugated, on an average of 4 cysteinyl, to monomethylauristatin E (MMAE), via a cleavable maleimidocaproyl-valyl-citrullinyl-p-aminobenzyloxycarbonyl (mc-val-cit-PABC) type linker

losatuzumab vedotin (116)

immunoglobulin G1-kappa, anti-[*Homo sapiens* EGFR (epidermal growth factor receptor, receptor tyrosine-protein kinase erbB-1, ERBB1, HER1, HER-1, ERBB) delta 2-7 isoform (delta2-7EGFR, de2-7 EGFR, EGFRvIII)], humanized and chimeric monoclonal antibody conjugated to auristatin E; humanized gamma1 heavy chain (1-446) [humanized VH (*Homo sapiens* IGHV4-30-4*01 (81.40%) -(IGHD)-IGHJ4*01) [9.7.9] (1-116) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 R120>K (213) (117-214), hinge (215-229), CH2 (230-339), CH3 E12 (355), M14 (357) (340-444), CHS (445-446)) (117-446)], (219-214')-disulfide with chimeric kappa light chain (1'-214') [*Mus musculus* V-KAPPA (IGKV14-100*01 (86.30%) -IGKJ1*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 A45.1 (153), V101 (191) (108'-214')]; dimer (225-225":228-228")-bisdisulfide; conjugated, on an average of 3 cysteinyl, to monomethylauristatin E (MMAE), via a cleavable maleimidocaproyl-valyl-citrullinyl-p-aminobenzyloxycarbonyl (mc-val-cit-PABC) type linker

lifastuzumab vedotin (110)

immunoglobulin G1-kappa auristatin E conjugate, anti-[*Homo sapiens* SLC34A2 (solute carrier family 34 sodium phosphate member 2, sodium/phosphate cotransporter 2B, NaPi2b, NaPi3b)], humanized monoclonal antibody conjugated to auristatin E; gamma1 heavy chain (1-450) [humanized VH (*Homo sapiens* IGHV3-23*04 (85.70%) -(IGHD)-IGHJ5*01) [8.8.13] (1-120) -*Homo sapiens* IGHG1*03 (CH1 R120>K (217) (121-218), hinge (219-233), CH2 (234-343), CH3 (344-448), CHS (449-450)) (121-450)], (223-219')-disulfide with kappa light chain (1'-219') [humanized V-KAPPA (*Homo sapiens* IGKV1-39*01 (78.00%) -IGKJ1*01) [11.3.9] (1'-112') -*Homo sapiens* IGKC*01 (113'-219')]; dimer (229-229":232-232")-bisdisulfide; conjugated, on an average of 3 to 4 cysteinyl, to monomethylauristatin E (MMAE), via a cleavable maleimidocaproylvalyl-citrullinyl-p-aminobenzyloxycarbonyl (mc-val-cit-PABC) type linker

pinatuzumab vedotin (108)

immunoglobulin G1-kappa auristatin E conjugate, anti-[*Homo sapiens* CD22 (sialic acid binding Ig-like lectin 2, SIGLEC2, SIGLEC-2, Blymphocyte cell adhesion molecule, BL-CAM, Leu-14)], humanized monoclonal antibody conjugated to auristatin E; gamma1 heavy chain (1-450) [humanized VH (*Homo sapiens* IGHV3-66*01 (79.60%) -(IGHD)-IGHJ4*01) [8.8.13] (1-120) -*Homo sapiens* IGHG1*03 (CH1 R120>K (217) (121-218), hinge (219-233), CH2 (234-343), CH3 (344-448), CHS (449-450)) (121-450)], (223-219')-disulfide (if not conjugated) with kappa light chain (1'-219') [humanized V-KAPPA (*Homo sapiens* IGKV1-39*01 (80.00%) -IGKJ1*01) [11.3.9] (1'-112') -*Homo sapiens* IGKC*01 (113'-219')]; dimer (229-229":232-232")-bisdisulfide; conjugated, on an average of 3 to 4 cysteinyl, to monomethylauristatin E (MMAE), via a cleavable maleimidocaproyl-valylcitrullinyl-p-aminobenzylcarbamate (mc-val-cit-PABC) linker

polatuzumab vedotin (110)

immunoglobulin G1-kappa auristatin E conjugate, anti-[*Homo sapiens* CD79B (immunoglobulin-associated CD79 beta)], humanized monoclonal antibody conjugated to auristatin E;

gamma1 heavy chain (1-447) [humanized VH (*Homo sapiens* IGHV3-23*04 (76.50%) - (IGHD)-IGHJ4*01) [8.8.10] (1-117) -*Homo sapiens* IGHG1*03 (CH1 R120>K (214)(118-215), hinge (216-230), CH2 (231-340), CH3 (341-445), CHS (446-447)) (118-447)], (220-218')-disulfide with kappa light chain (1'-218') [humanized V-KAPPA (*Homo sapiens* IGKV1-39*01 (85.90%) -IGKJ1*01) [10.3.9] (1'-111') -*Homo sapiens* IGKC*01 (112'-218')]; dimer (226-226":229-229")-bisdisulfide; conjugated, on an average of 3 to 4 cysteinyl, to monomethylauristatin E (MMAE), via a cleavable maleimidocaproyl-valyl-citrullinyl-p-aminobenzyloxycarbonyl (mc-val-cit-PABC) type linker

samrotamab vedotin (118)

immunoglobulin G1-kappa, anti-[*Homo sapiens* LRRC15 (leucine-rich repeat-containing protein 15, leucine-rich repeat induced by beta-amyloid homolog, LIB)], humanized and chimeric monoclonal antibody conjugated to auristatin E;

gamma1 heavy chain (1-450) [humanized VH (*Homo sapiens* IGHV1-2*02 (77.6%) - (IGHD) - IGHJ5*01 (86.7%)) [8.8.13] (1-120) -*Homo sapiens* IGHG1*01 (CH1 (121-218), hinge (219-233), CH2 (234-343), CH3 (344-448), CHS (449-450)) (121-450)], (223-214')-disulfide with kappa light chain chimeric (1'-214') [*Mus musculus* V-KAPPA (IGKV10-96*01 (85.30%) - IGKJ1*01 (91.7%)/*Homo sapiens* IGKV1-39*01 (84.2%) -IGKJ4*01 (100%)] [6.3.9] (1'-107') -*Homo sapiens* IGKC*01,Km3 A45.1 (153), V101 (191)(108'-214')]; dimer (229-229":232-232")-bisdisulfide; conjugated, on an average of 2 cysteinyl, to monomethylauristatin E (MMAE), via a cleavable maleimidocaproyl-valyl-citrullinyl-p-aminobenzyloxycarbonyl (mc-val-cit-PABC) type linker

sirtratumab vedotin (117)

immunoglobulin G2-kappa, anti-[*Homo sapiens* SLITRK6 (SLIT and NTRK like family member 6)], *Homo sapiens* monoclonal antibody conjugated to auristatin E;

gamma2 heavy chain (1-446) [*Homo sapiens* VH (IGHV3-33*01 (96.90%) - (IGHD) - IGHJ6*01) [8.8.13] (1-120) -IGHG2*01, G2m.. (CH1 (121-218), hinge (219-230), CH2 V45.1 (281) (231-339), CH3 (340-444), CHS (445-446)) (121-446)], (134-219')-disulfide with kappa light chain (1'-219') [*Homo sapiens* V-KAPPA (IGKV2-28*01 (93.00%) -IGKJ1*01) [11.3.9] (1'-112') -IGKC*01, Km3 A45.1 (158), V101 (196) (113'-219')]; dimer (222-222":223-223":226-226":229-229")-tetrakisdisulfide; conjugated, on an average of 4 cysteinyl, to monomethylauristatin E (MMAE), via a cleavable maleimidocaproyl-valyl-citrullinyl-p-aminobenzyloxycarbonyl (mc-val-cit-PABC) type linker

sofituzumab vedotin (110)

immunoglobulin G1-kappa auristatin E conjugate, anti-[*Homo sapiens* MUC16 (mucin 16, MUC-16, cancer antigen 125, CA125)], humanized monoclonal antibody conjugated to auristatin E;

gamma1 heavy chain (1-446) [humanized VH (*Homo sapiens* IGHV3-48*03 (79.80%) - (IGHD)-IGHJ4*01) [9.8.9] (1-116) -*Homo sapiens* IGHG1*03 (CH1 R120>K (213) (117-214), hinge (215-229), CH2 (230-339), CH3 (340-444), CHS (445-446)) (117-446)], (219-214')-disulfide with kappa light chain (1'-214') [humanized V-KAPPA (*Homo sapiens* IGKV1-5*01 (87.90%) -IGKJ1*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01 (108'-214')]; dimer (225-225":228-228")-bisdisulfide; conjugated, on an average of 3 to 4 cysteinyl, to monomethylauristatin E (MMAE), via a cleavable maleimidocaproylvalyl-citrullinyl-p-aminobenzyloxycarbonyl (mc-val-cit-PABC) type linker

telisotuzumab vedotin (115)

immunoglobulin G1-kappa, anti-[*Homo sapiens* MET (met proto-oncogene, hepatocyte growth factor (HGF) receptor, HGFR, scatter factor (SF) receptor, HGF/SF receptor, receptor tyrosine-protein kinase c-met, papillary renal cell carcinoma 2, RCCP2)], humanized monoclonal antibody conjugated to auristatin E;

gamma1 heavy chain (1-445) [humanized VH (*Homo sapiens* IGHV1-2*02 (92.90%) -(IGHD)-IGHJ4*01) [8.8.11] (1-118) -*Homo sapiens* IGHG1*03, G1m3 (CH1 (119-216), hinge K7>del, T8>C (223), T10>del (217-229), CH2 (230-339), CH3 (340-444), CHS K>del (445)) (119-445)], (221-218')-disulfide with kappa light chain (1'-218') [humanized V-KAPPA (*Homo sapiens* IGKV4-1*01 (85.10%) -IGKJ4*01) [10.3.9] (1'-111') -*Homo sapiens* IGKC*01, Km3 (112'-218')]; dimer (223-223":225-225":228:228")-trisulfide; conjugated, on an average of 3 cysteinyl, to monomethylauristatin E (MMAE), via a cleavable maleimidocaproyl-valyl-citrullinyl-*p*-aminobenzyloxycarbonyl (mc-val-cit-PABC) type linker

tisotumab vedotin (113)

immunoglobulin G1-kappa, anti-[*Homo sapiens* F3 (coagulation factor III (thromboplastin, tissue factor), CD142)], *Homo sapiens* monoclonal antibody conjugated to auristatin E;

gamma1 heavy chain (1-448) [*Homo sapiens* VH (IGHV3-23*01 (93.90%) -(IGHD)-IGHJ5*01) [8.8.11] (1-118) -IGHG1*03, G1m3 (CH1 (119-216), hinge (217-231), CH2 (232-341), CH3 (342-446), CHS (447-448)) (119-448)], (221-214')-disulfide with kappa light chain (1'-214') [*Homo sapiens* V-KAPPA (IGKV1D-16*01 (96.80%) -IGKJ2*01) [6.3.9] (1'-107') -IGKC*01, Km3 (108'-214')]; dimer (227-227":230-230")-bisulfide; conjugated, on an average of 3 to 4 cysteinyl, to monomethylauristatin E (MMAE), via a cleavable maleimidocaproyl-valyl-citrullinyl-*p*-aminobenzyloxycarbonyl (mc-val-cit-PABC) type linker

vandortuzumab vedotin (112)

immunoglobulin G1-kappa, anti-[*Homo sapiens* STEAP1 (six-transmembrane epithelial antigen of the prostate 1, PRSS24, STEAP)], humanized monoclonal antibody;

gamma1 heavy chain (1-454) [humanized VH (*Homo sapiens* IGHV3-48*03 (80.80%) -(IGHD)-IGHJ4*01) [9.7.17] (1-124) -*Homo sapiens* IGHG1*03 (CH1 R120>K (221) (125-222), hinge (223-237), CH2 (238-347), CH3 (348-452), CHS (453-454)) (125-454)], (227-220')-disulfide with kappa light chain (1'-220') [humanized V-KAPPA (*Homo sapiens* IGKV1-16*01 (81.20%) -IGKJ1*01) [12.3.9] (1'-113') -*Homo sapiens* IGKC*01 (114'-220')]; dimer (233-233":236-236")-bisulfide; conjugated, on an average of 3 to 4 cysteinyl, to monomethylauristatin E (MMAE), via a cleavable maleimidocaproyl-valyl-citrullinyl-*p*-aminobenzyloxycarbonyl (mc-val-cit-PABC) type linker

-mab & -tecan (for antineoplastics, topoisomerase I inhibitors)

trastuzumab deruxtecan (116)

immunoglobulin G1-kappa, anti-[*Homo sapiens* ERBB2 (epidermal growth factor receptor 2, receptor tyrosine-protein kinase erbB-2, EGFR2, HER2, HER-2, p185c-erbB2, NEU, CD340)], humanized monoclonal antibody conjugated to deruxtecan, comprising a linker and a camptothecin derivative;

gamma1 heavy chain (1-450) [humanized VH (*Homo sapiens* IGHV3-66*01 (81.60%) -(IGHD)-IGHJ4*02) [8.8.13] (1-120) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 R120>K (217) (121-218), hinge (219-233), CH2 (234-343), CH3 E12 (359), M14 (361) (344-448), CHS (449-450)) (121-450)], (223-214')-disulfide with kappa light chain (1'-214') [humanized V-KAPPA (*Homo sapiens* IGKV1-39*01 (86.20%) -IGKJ1*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 A45.1, V101 (108'-214')]; dimer (229-229":232-232")-bisulfide; conjugated, on an average of 8 cysteinyl, to deruxtecan, comprising a linker and a camptothecin derivative.

deruxtecan

(3*RS*)-1-[(10*S*)-10-benzyl-1-[[[(1*S*,9*S*)-9-ethyl-5-fluoro-9-hydroxy-4-methyl-10,13-dioxo-2,3,9,10,13,15-hexahydro-1*H*,12*H*-benzo[*de*]pyrano [3',4':6,7]indolizino[1,2-*b*]quinolin-1-yl]amino]-1,6,9,12,15,18-hexaoxo-3-oxa-5,8,11,14,17-pentaazatricosan-23-yl]-2,5-dioxopyrrolidin-3-yl

labetuzumab govitecan (113)

immunoglobulin G1-kappa, anti-[*Homo sapiens* CEACAM5 (carcinoembryonic antigen-related cell adhesion molecule 5, CEA, CD66e)], monoclonal antibody conjugated to 7-ethyl-10-hydroxycamptothecin (SN-38), active metabolite of irinotecan;

gamma1 heavy chain (1-449) [humanized VH (*Homo sapiens* IGHV3-48*01 (75.30%) - (IGHD)-IGHJ5*01) [8.8.12] (1-119) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (120-217), hinge (218-232), CH2 (233-342), CH3 (343-447), CHS (448-449)) (120-449)], (222-213')-disulfide with kappa light chain (1'-213') [humanized V-KAPPA (*Homo sapiens* IGKV1-39*01 (85.70%) -IGKJ1*01) [6.3.8] (1'-106') -*Homo sapiens* IGKC*01, Km3 (107'-213')]; dimer (228-228":231-231")-bisdisulfide;

conjugated, on an average of 6 cysteinyl, to 7-ethyl-10-hydroxycamptothecin (SN-38), active metabolite of irinotecan (CPT-11, camptothecin-11), via a maleimide-type cleavable linker (carbonate group, 4-aminobenzyl alcohol and cathepsine-B-cleavable dipeptide Phe-Lys) and containing a triazoline group and a spacer PEG (n=8)

govitecan

(3*RS*)-1-[(4-[[[1-[(34*S*)-38-amino-34-[(4-[[[[(4*S*)-4,11-diethyl-9-hydroxy-3,14-dioxo-3,4,12,14-tetrahydro-1*H*-pyrano[3',4':6,7]indolizino[1,2-*b*]quinolin-4-yl]oxy}carbonyl]oxy]methyl}phenyl]carbamoyl]-28,32-dioxo-3,6,9,12,15,18,21,24,30-nonaoxa-27,33-diazaoctatriacontan-1-yl]-1*H*-1,2,3-triazol-4-yl)methyl]carbamoyl}cyclohexyl)methyl]-2,5-dioxopyrrolidin-3-yl

sacituzumab govitecan (113)

immunoglobulin G1-kappa, anti-[*Homo sapiens* TACSTD2 (tumor-associated calcium signal transducer 2, membrane component chromosome 1 surface marker 1, M1S1, gastrointestinal tumor-associated antigen GA7331, pancreatic carcinoma marker protein GA733-1, epithelial glycoprotein-1, EGP-1, trophoblast antigen-2, cell surface glycoprotein Trop-2, TROP2)], humanized monoclonal antibody conjugated to 7-ethyl-10-hydroxycamptothecin (SN-38), active metabolite of irinotecan;

gamma1 heavy chain (1-451) [humanized VH (*Homo sapiens* IGHV7-4-1*02 (85.70%) - (IGHD)-IGHJ2*01) [8.8.14] (1-121) -*Homo sapiens* IGHG1*03, Gm3 (CH1 (122-219), hinge (220-234), CH2 (235-344), CH3 (345-449), CHS (450-451)) (122-451)], (224-214')-disulfide with kappa light chain (1'-214') [humanized V-KAPPA (*Homo sapiens* IGKV1-9*01 (82.20%) -IGKJ4*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimer (230-230":233-233")-bisdisulfide;

conjugated, on an average of 6 cysteinyl, to 7-ethyl-10-hydroxycamptothecin (SN-38), active metabolite of irinotecan (CPT-11, camptothecin-11), via a maleimide-type cleavable linker (carbonate group, 4-aminobenzyl alcohol and cathepsine-B-cleavable dipeptide Phe-Lys) and containing a triazoline group and a spacer PEG (n=8)

govitecan (for *govitecan*, please refer to *labetuzumab govitecan (113)*)

-mab & ozogamicin

gemtuzumab ozogamicin (115)

immunoglobulin G4-kappa, anti-[*Homo sapiens* CD33 (sialic acid binding Ig-like lectin 3, SIGLEC3, SIGLEC-3, gp67, p67)], humanized monoclonal antibody conjugated to *N*-acetyl-

gamma calicheamicin;
gamma4 heavy chain (1-443) [humanized VH (*Homo sapiens* IGHV1-3*01 (72.90%) -(IGHD) -IGHJ5*01) [8.8.9] (1-116)), IGHG4*01 (CH1 (117-214), hinge S10>P (224) (215-226), CH2 (227-336), CH3 (337-441), CHS (442-443)) (117-443)], (130-218')-disulfide with kappa light chain (1'-218') [humanized V-KAPPA (*Homo sapiens* IGKV1-5*01 (81.90%) -IGKJ1*01) [10.3.9] (1'-111') -*Homo sapiens* IGKC*01, Km3 (112'-218')]; dimer (232-232":235-235")-bisdisulfide; conjugated, on an average of 2 or 3 lysyl (0-6), to *N*-acetyl-*S'*-des(methylsulfanyl)-*S'*-(4-hydrazinyl-2-methyl-4-oxobutan-2-yl)calicheamicin γ_1 via a bifunctional 4-(4-acetylphenoxy)butanoyl (AcBut) linker

inotuzumab ozogamicin (92)

immunoglobulin G4, anti-(human CD22 (antigen)) (human-mouse monoclonal G544 heavy chain), disulfide with human-mouse monoclonal G544 κ -chain, dimer, conjugate with methyl *N*-{(1*R*,4*Z*,8*S*,13*E*)-8-(4,6-dideoxy-4-{{(4-*S*-{4-[(6-deoxy-3-*O*-methyl- α -*L*-mannopyranosyl)oxy]-3-iodo-5,6-dimethoxy-2-methylbenzoyl}-4-thio- β -*D*-ribohexopyranosyl)oxy]amino}-2-*O*-[4-(*N*-ethylacetamido)-2,4-dideoxy-3-*O*-methyl- α -*L*-threopentopyranosyl]- β -*D*-glucopyranosyloxy)-13-[2-({4-[2-(1-{{4-(4-amino-4-oxobutyl)oxy]phenyl}ethylidene)hydrazinyl]-2-methyl-4-oxobutan-2-yl}disulfanyl)ethylidene)-1-hydroxy-11-oxobicyclo[7.3.1]trideca-4,9-diene-2,6-diyn-10-yl}carbamate

-mab & talirine

serclutamab talirine (120)

immunoglobulin G1-kappa, anti-[*Homo sapiens* EGFR (epidermal growth factor receptor, receptor tyrosine-protein kinase erbB-1, ERBB1, HER1, HER-1, ERBB)], monoclonal antibodyconjugated to the pyrrolobenzodiazepine (PDB) dimer SGD-1882;
gamma1 heavy chain (1-446) [VH (*Homo sapiens* IGHV4-30-4*01 (81.4%) -(IGHD) -IGHJ4*01 (92.9%)) [9.7.9] (1-116) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 R120>K (213) (117-214), hinge (215-229), CH2 S3>C (238) (230-339), CH3 E12 (355), M 14 (357) (340-444), CHS (445-446)) (117-446)], (219-214')-disulfide with kappa light chain (1'-214') [V-KAPPA (**Error! Hyperlink reference not valid.***Mus musculus* IGKV14-100*01 (86.3%) -IGKJ1*01 (100%)/*Homo sapiens* IGKV1-12*01 (74.7%) -IGKJ4*01 (90.9%)) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')]; dimer (225-225":228-228")-bisdisulfide; conjugated, on two site-specific drug attachment engineered cysteines (C238, C238"), to pyrrolobenzodiazepine (PDB) dimers SGD-1882, via a cathepsin-cleavable maleimidocaproyl-valine-alanine (MC-Val-Ala) type linker

talirine

S^{239}, S^{239} -bis[(2^{11a}*S*,8^{11a}*S*,12*S*,15*S*,23³*RS*)-1⁴,2⁷,8⁷-trimethoxy-12-methyl-2⁵,8⁵,11,14,17,23²,23⁵-heptaoxo-15-(propan-2-yl)-2⁵,2^{11a},8⁵,8^{11a}-tetrahydro-2¹*H*,8¹*H*-3,7-dioxa-10,13,16-triaza-2(2,8),8(8,2)-bis(pyrrolo[2,1-*c*][1,4]benzodiazepina)-23(1)-pyrrolidina-1(1),9(1,4)-dibenzenatricosaphan-23³-yl]

vadastuximab talirine (113)

immunoglobulin G1-kappa, anti-[*Homo sapiens* CD33 (sialic acid binding Ig-like lectin 3, SIGLEC3, SIGLEC-3, gp67, p67)], chimeric monoclonal antibody conjugated to the pyrrolobenzodiazepine (PDB) dimer SGD-1882;
gamma1 heavy chain (1-447) [*Mus musculus* VH (IGHV1-85*01 -(IGHD)-IGHJ4*01) [8.8.10] (1-117) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (118-215), hinge (216-230), CH2 S3>C (239) (231-340), CH3 (341-445), CHS (446-447)) (118-447)], (220-214')-disulfide with kappa light chain (1'-214') [*Mus musculus* V-KAPPA (IGKV14-111*01 -*Homo sapiens* IGKJ4*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimer (226-226":229-229")-bisdisulfide; conjugated, on two site-specific drug attachment engineered cysteines (C239,

C239"), to a maximum of 2 pyrrolobenzodiazepine (PDB) dimers SGD-1882, each via a cleavable (valine-alanine dipeptide as cathepsine B cleavage site) maleimidocaproyl type linker

-mab & -tansine³¹

trastuzumab emtansine (103)

immunoglobulin G1-kappa, anti-[*Homo sapiens* ERBB2 (epidermal growth factor receptor 2, HER-2, p185c-erbB2, NEU, EGFR2)], humanized monoclonal antibody conjugated to maytansinoid DM1;
gamma1 heavy chain (1-449) [humanized VH (*Homo sapiens* IGHV3-66*01 (81.60%) - (IGHD)-IGHJ6*01 T123>L) [8.8.13] (1-120) -*Homo sapiens* IGHG1*03 (121-449) CH1 R120>K), (223-214')-disulfide with kappa light chain (1'-214') [humanized V-KAPPA (*Homo sapiens* IGKV1-39*01 (86.30%) -IGKJ1*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01 (108'-214')]; (229-229":232-232")-bisdisulfide dimer; conjugated, on an average of 3 to 4 lysyl, to maytansinoid DM1 via a succinimidyl-4-(*N*-maleimidomethyl) cyclohexane-1-carboxylate (SMCC) linker

laprituximab emtansine (114)

immunoglobulin G1-kappa, anti-[*Homo sapiens* EGFR (epidermal growth factor receptor, receptor tyrosine-protein kinase erbB-1, ERBB1, HER1, HER-1, ERBB)], chimeric monoclonal antibody conjugated to maytansinoid DM1; gamma1 heavy chain (1-448) [*Mus musculus* VH (IGHV1-7*01 -(IGHD)-IGHJ4*01) [8.8.12] (1-119) -*Homo sapiens* IGHG1*01, Gm17,1 (CH1 (120-217), hinge (218-232), CH2 (233-342), CH3 (343-447), CHS K2>del (448) (120-448)), (222-214')-disulfide with kappa light chain (1'-214') [*Mus musculus* V-KAPPA (IGKV19-93*01-IGKJ2*03) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimer (228-228":231-231")-bisdisulfide; conjugated, on an average of 3 to 4 lysyl, to maytansinoid DM1 via a succinimidyl-4-(*N*-maleimidomethyl) cyclohexane-1-carboxylate (SMCC) linker forming a nonreducible thioether bond

naratuximab emtansine (114)

immunoglobulin G1-kappa, anti-[*Homo sapiens* CD37 (tetraspanin-26, TSPAN26)], chimeric monoclonal antibody conjugated to maytansinoid DM1;
gamma1 heavy chain (1-444) [*Mus musculus* VH (IGHV2-3*01 -(IGHD)- IGHJ3*01) [8.7.9] (1-115) -*Homo sapiens* IGHG1*01, Gm17,1 (CH1 (116-213), hinge (214-228), CH2 (229-338), CH3 (339-443), CHS K2>del (444)) (116-444)], (218-214')-disulfide with kappa light chain (1'-214') [*Mus musculus* V-KAPPA (IGKV12-46*01 - IGKJ1*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimer (224-224":227-227")-bisdisulfide; conjugated, on an average of 3 to 4 lysyl, to maytansinoid DM1 via a succinimidyl-4-(*N*-maleimidomethyl) cyclohexane-1-carboxylate (SMCC) linker forming a nonreducible thioether bond

cantuzumab mertansine (105)

immunoglobulin G1-kappa, anti-[*Homo sapiens* MUC1 sialylated carbohydrate, tumour-associated (CA242, cancer antigen 242)], humanized monoclonal antibody conjugated to maytansinoid DM1;
gamma1 heavy chain (1-449) [humanized VH (*Homo sapiens* IGHV7-4-1*02 (76.50%) - (IGHD)-IGHJ2*01 R120>Q (111), L123>T (114)) [8.8.12] (1-119) -*Homo sapiens* IGHG1*01 (120-449)], (222-219')-disulfide with kappa light chain (1'-219') [humanized V-KAPPA (*Homo sapiens* IGKV2-28*01 (82.00%) -IGKJ3*01 V124>L (109), D125>E (110), I126>L

³¹ The names ending in *-tansine* and the descriptions are published in Annex 4.2 of "International Nonproprietary Names (INN) for pharmaceutical substances. Names for radicals, groups & others: comprehensive list (WHO/EMP/RHT/TSN/2015.1)".

(111)) [11.3.9] (1'-112') -*Homo sapiens* IGKC*01 (113'-219')]; (228-228":231-231")-bisdisulfide dimer; conjugated, on an average of 4 lysyl, to maytansinoid DM1 [*N*²-deacetyl-*N*²-(3-mercapto-1-oxopropyl)-maytansine] via the reducible SPP linker [*N*-succinimidyl 4-(2-pyridyldithio)pentanoate]

lorvotuzumab mertansine (103)

immunoglobulin G1-kappa, anti-[*Homo sapiens* NCAM1 (neural cell adhesion molecule 1, CD56, NCAM-1)], humanized monoclonal antibody conjugated to maytansinoid DM1; gamma1 heavy chain (1-448) [humanized VH (*Homo sapiens* IGHV3-30*03 (91.80%) - (IGHD)-IGHJ4*01) [8.8.11] (1-118) -*Homo sapiens* IGHG1*01 (119-448)], (221-219')-disulfide with kappa light chain (1'-219') [humanized V-KAPPA (*Homo sapiens* IGKV2-30*02 (92.00%) -IGKJ1*01) [11.3.9] (1'-112') -*Homo sapiens* IGKC*01 (113'-219')]; (227-227":230-230")-bisdisulfide dimer; conjugated, on an average of 3 to 4 lysyl, to maytansinoid DM1 via a thiopentanoate linker

anetumab ravtansine (109)

immunoglobulin G1-lambda2, anti-[*Homo sapiens* MSLN (mesothelin, pre-pro-megakaryocyte-potentiating factor, megakaryocyte potentiating factor, MPF, CAK1)], *Homo sapiens* monoclonal antibody conjugated to maytansinoid DM4; gamma1 heavy chain (1-450) [*Homo sapiens* VH (IGHV5-51*01 (94.90%) - (IGHD)-IGHJ4*01) [8.8.13] (1-120) -IGHG1*01 (CH1 (121-218), hinge (219-233), CH2 (234-343), CH3 (344-448), CHS (449-450)) (121-450)], (223-216')-disulfide with lambda light chain (1'-217') [*Homo sapiens* V-LAMBDA (IGLV2-14*01 (95.60%) -IGLJ2*01) [9.3.11] (1'-111') -IGLC2*01 A43>G (155) (112'-217')]; dimer (229-229":232-232")-bisdisulfide; conjugated, on an average of 3 lysyl, to maytansinoid DM4 [*N*²-deacetyl-*N*²-(4-mercapto-4-methyl-1-oxopentyl)-maytansine] via the reducible SPDB linker [*N*-succinimidyl 4-(2-pyridyldithio)butanoate]

cantuzumab ravtansine (105)

immunoglobulin G1-kappa, anti-[*Homo sapiens* MUC1 sialylated carbohydrate, tumour-associated (CA242, cancer antigen 242)], humanized monoclonal antibody conjugated to maytansinoid DM4; gamma1 heavy chain (1-449) [humanized VH (*Homo sapiens* IGHV7-4-1*02 (76.50%) - (IGHD)-IGHJ2*01 R120>Q (111), L123>T (114)) [8.8.12] (1-119) -*Homo sapiens* IGHG1*01 (120-449)], (222-219')-disulfide with kappa light chain (1'-219') [humanized V-KAPPA (*Homo sapiens* IGKV2-28*01 (82.00%) -IGKJ3*01 V124>L (109),D125>E (110), I126>L (111)) [11.3.9] (1'-112') -*Homo sapiens* IGKC*01 (113'-219')]; (228-228":231-231")-bisdisulfide dimer; conjugated, on an average of 3 to 4 lysyl, to maytansinoid DM4 [*N*²-deacetyl-*N*²-(4-mercapto-4-methyl-1-oxopentyl)-maytansine] via the reducible SPDB linker [*N*-succinimidyl 4-(2-pyridyldithio)butanoate]

coltuximab ravtansine (109)

immunoglobulin G1-kappa, anti-[*Homo sapiens* CD19 (B lymphocyte surface antigen B4, Leu-12)], chimeric monoclonal antibody conjugated to maytansinoid DM4; gamma1 heavy chain (1-450) [Mus musculus VH (IGHV1-69*02 - (IGHD)-IGHJ4*01) [8.8.13] (1-120) -*Homo sapiens* IGHG1*01 (CH1 (121-218), hinge (219-233), CH2 (234-343), CH3 (344-448), CHS (449-450)) (121-450)], (223-211')-disulfide with kappa light chain (1'-211') [Mus musculus V-KAPPA (IGKV4-70*01 -IGKJ1*01) [5.3.7] (1'-104') -*Homo sapiens* IGKC*01 (105'-211')]; dimer (229-229":232-232")-bisdisulfide; conjugated, on an average of 3 to 4 lysyl, to maytansinoid DM4 [*N*²-deacetyl-*N*²-(4-mercapto-4-methyl-1-oxopentyl)-maytansine] via the reducible SPDB linker [*N*-succinimidyl 4-(2-pyridyldithio)butanoate]

indatuximab ravtansine (105)

immunoglobulin G4-kappa, anti-[*Homo sapiens* SDC1 (syndecan-1, CD138)], chimeric monoclonal antibody conjugated to maytansinoid DM4;
gamma4 heavy chain (1-449) [*Mus musculus* VH (IGHV1-9*01 - (IGHD)-IGHJ4*01) [8.8.15] (1-122) -*Homo sapiens* IGHG4*01 (123-449)], (136-214')-disulfide with kappa light chain (1'-214') [*Mus musculus* V-KAPPA (IGKV10-94*01 -IGKJ1*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01 (108'-214')]; (228-228":231-231")-bisdisulfide dimer; conjugated, on an average of 3 to 4 lysyl, to maytansinoid DM4 [*N*²-deacetyl-*N*²-(4-mercapto-4-methyl-1-oxopentyl)-maytansine] via the reducible SPDB linker [*N*-succinimidyl 4-(2-pyridyldithio)butanoate]

mirvetuximab soravtansine (113)

immunoglobulin G1-kappa, anti-[*Homo sapiens* FOLR1 (folate receptor 1, folate receptor alpha, FR-alpha, adult folate-binding protein, FBP, ovarian tumor-associated antigen MOv18)], chimeric monoclonal antibody conjugated to maytansinoid DM4;
gamma1 heavy chain (1-447) [*Mus musculus* VH (IGHV1-37*01 - (IGHD)-IGHJ4*01) [8.8.11] (1-118) -*Homo sapiens* IGHG1*01, G1m17,1 (CH1 (119-216), hinge (217-231), CH2 (232-341), CH3 (342-446), CHS K2>del (447)) (119-447)], (221-218')-disulfide with kappa light chain (1'-218') [*Mus musculus* V-KAPPA (IGKV3-9*01 -IGKJ2*01) [10.3.9] (1'-111') -*Homo sapiens* IGKC*01, Km3 (112'-218')]; dimer (227-227":230-230")-bisdisulfide; conjugated, on an average of 3 or 4 lysyl, to maytansinoid DM4 [*N*²-deacetyl-*N*²-(4-mercapto-4-methyl-1-oxopentyl)-maytansine] via the reducible sulfo-SPDB linker [*N*-succinimidyl 4-(2-pyridyldithio)-2-sulfobutanoate]

soravtansine

(2*RS*)-4-[2-(5-{[(2*S*)-1-{{[(1*S*,2*R*,3*S*,5*S*,6*S*,16*E*,18*E*,20*R*,21*S*)-11-chloro-21-hydroxy-12,20-dimethoxy-2,5,9,16-tetramethyl-8,23-dioxo-4,24-dioxo-9,22-diazatetracyclo[19.3.1.1^{10,14}.0^{3,5}]hexacos-10,12,14(26),16,18-pentaen-6-yl]oxy}-1-oxopropan-2-yl](methyl)amino}-2-methyl-5-oxopentan-2-yl)disulfanyl]-2-sulfobutanoyl

-mab & tesirine

camidanlumab tesirine (117)

immunoglobulin G1-kappa, anti-[*Homo sapiens* IL2RA (interleukin 2 receptor alpha subunit, IL-2RA, TAC, p55, CD25)], *Homo sapiens* monoclonal antibody conjugated to the pyrrolbenzodiazepine (PBD) dimer SCX;
gamma1 heavy chain (1-445) [*Homo sapiens* VH (IGHV1-69*02 (94.90%) - (IGHD) - IGHJ4*01) [8.8.8] (1-115) -*Homo sapiens* IGHG1*03, G1m3, nG1m1 (CH1 R120 (212) (116-213), hinge (214-228), CH2 (229-338), CH3 E12 (354), M14 (356) (339-443), CHS (444-445)) (116-445)], (218-214')-disulfide with kappa light chain (1'-214') [*Homo sapiens* V-KAPPA (IGKV3-20*01 (99.00%) -IGKJ4*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 A45.1 (153), V101 (191) (108'-214')]; dimer (224-224":227-227")-bisdisulfide; conjugated, on an average of 2 cysteines, to the pyrrolbenzodiazepine (PBD) dimer SCX, via a cleavable (valine-alanine dipeptide as cathepsin B cleavage site) maleimide type linker containing a spacer PEG (n=8)

tesirine

(1^{11a}*S*,9¹¹*S*,9^{11a}*S*,16*S*,19*S*,52³*RS*)-9¹¹-hydroxy-1⁷,9⁷-dimethoxy-1²,9²,16-trimethyl-1⁵,9⁵,10,15,18,21,49,52⁵,52⁵-nonaaxo-19-(propan-2-yl)-1⁵,1^{11a},9¹¹,9^{11a}-tetrahydro-1¹*H*,9¹*H*,9⁵*H*-2,8,11,24,27,30,33,36,39,42,45-undecaaxo-14,17,20,48-tetraaxo-1(8),9(8,10)-bis(pyrrolo[2,1-*c*][1,4]benzodiazepina)-52(1)-pyrrolidina-13(1,4)benzenadopentacontaphan-52³-yl

loncastuximab tesirine (117)

immunoglobulin G1-kappa, anti-[*Homo sapiens* CD19 (B lymphocyte surface antigen B4, Leu-12)], chimeric monoclonal antibody conjugated to the pyrrolbenzodiazepine (PBD) dimer SCX;

gamma1 heavy chain (1-449) [*Mus musculus* VH (IGHV1-69*02 (85.70%) -(IGHD) -IGHJ4*01) [8.8.13] (1-120) -*Homo sapiens* IGHG1*03v, G1m3>G1m17, nG1m1 (CH1 R120>K (217) (121-218), hinge (219-233), CH2 (234-343), CH3 E12 (359), M14 (361) (344-448), CHS K2>del (449)) (121-449)], (223-211')-disulfide with kappa light chain (1'-211') [*Mus musculus* V-KAPPA (IGKV4-70*01 (91.40%) -IGKJ1*01) [5.3.7] (1'-104') -*Homo sapiens* IGKC*01, Km3 A45.1 (150), V101 (188) (105'-211')]; dimer (229-229":232-232")-bisdisulfide; conjugated, on an average of 2 cysteines, to the pyrrolbenzodiazepine (PBD) dimer SCX, via a cleavable (valine-alanine dipeptide as cathepsine B cleavage site) maleimide type linker containing a spacer PEG (n=8)

tesirine (for *tesirine*, please refer to *camidanlumab tesirine* (117))

rovalpituzumab tesirine (113)

immunoglobulin G1-kappa, anti-[*Homo sapiens* DLL3 (delta-like ligand 3)], humanized monoclonal antibody conjugated to the pyrrolbenzodiazepine (PBD) dimer SCX; gamma1 heavy chain (1-447) [humanized VH (*Homo sapiens* IGHV1-18*01 (86.700%) -(IGHD)-IGHJ4*01) [8.8.11] (1-118) -*Homo sapiens* IGHG1*01 G1m17,1 (CH1 (119-216), hinge (217-231), CH2 (232-341), CH3 (342-446), CHS K2>del (447)) (119-447)], (221-214')-disulfide with kappa light chain (1'-214') [humanized V-KAPPA (*Homo sapiens* IGKV3-15*01 (87.40%) -IGKJ2*01) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01, Km3 (108'-214')]; dimer (227-227":230-230")-bisdisulfide; conjugated, on an average of 2 cysteines, to the pyrrolbenzodiazepine (PBD) dimer SCX, via a cleavable (valine-alanine dipeptide as cathepsine B cleavage site) maleimide type linker containing a spacer PEG (n=8)

tesirine (for *tesirine*, please refer to *camidanlumab tesirine* (117))

-mab & chelating agents:

-xetan³²

lutetium (¹⁷⁷Lu) *lilotomab satetraxetan* (112)

immunoglobulin G1-kappa, anti-[*Homo sapiens* CD37 (TSPAN26, tetraspanin-26)], *Mus musculus* monoclonal antibody, lutetium (Lu 177) radiolabelled satetraxetan (DOTA derivative) conjugate;

gamma1 heavy chain (1-443) [*Mus musculus* VH (IGHV1S135*01 (96.90%) -(IGHD)-IGHJ4*01) [8.8.12] (1-119) -IGHG1*01 (CH1 E84>Q (177), P95>T (193), R96>W (194) (120-216), hinge (217-229), CH2 (230-336), CH3 N84.2>D (395), N84.4>D (397) (337-441), CHS (442-443)) (120-443)], (221-214')-disulfide with kappa light chain (1'-214') [*Mus musculus* V-KAPPA (IGKV6-25*01 (93.70%) -IGKJ4*01) [6.3.9] (1'-107') -IGKC*01 (108'-214')]; dimer (223-223":226-226":228-228")-trisdisulfide, an average of 1 to 2 amino groups (N⁶ of lysines) are substituted:

N-[*rac*-(4-{[(2*R*)-1,4,7,10-tetrakis(carboxymethyl)-1,4,7,10-tetraazacyclododecan-2-yl]methyl}phenyl)carbamoithiyl] (¹⁷⁷Lu)lutetium(3+) chelate

Other chelating agents:

³² The names ending in *-xetan* and the descriptions are published in "International Nonproprietary Names (INN) for pharmaceutical substances. Names for radicals, groups & others: comprehensive list (WHO/EMP/RHT/TSN/2015.1)".

cetuximab sarotalocan (120)

immunoglobulin G1-kappa, anti-*[Homo sapiens* EGFR (epidermal growth factor receptor, avian erythroblastic leukemia viral (v-erb-b) oncogene homolog, ERBB)], chimeric monoclonal antibody conjugated to IRDye 700DX (IR700) near-infrared photosensitizing dye; gamma1 heavy chain chimeric (1-449) [VH (*Mus musculus* IGHV2-2*03 (93.8%) -(IGHD) - IGHJ3*01 (100%)) [8.7.13] (1-119) -*Homo sapiens* IGHG1*03 (100%), G1m3, nG1m1 (CH1 R120 (216) (120-217), hinge (218-232), CH2 (233-342), CH3 E12 (358), M14 (360) (343-447), CHS (448-449)) (120-449)], (222-214')-disulfide with kappa light chain chimeric (1'-214') [V-KAPPA (*Mus musculus* IGKV5-48*01 (95.8%) -IGKJ5*01 (100%)) [6.3.9] (1'-107') -*Homo sapiens* IGKC*01 (100%), Km3 A45.1 (153), V101 (191) (108'-214')]; dimer (228-228":231-231")-bisdisulfide; conjugated on an average of 2 or 3 lysyl to photosensitizing dye IRDye 700DX

sarotalocan

6-({[3-((OC-6-13)-bis({3-[bis(3-sulfopropyl)(3-sulfonatopropyl)azaniumyl]propyl}dimethylsilanolato-κO,κO')[(phtalocyaninato(2)-κ4N29,N30,N31,N32)-1-yl]silicon}oxy)propoxy]carbonyl}amino)hexanoyl

Others:

mipsagargin (110)

sarcoplasmic/endoplasmic reticulum Ca²⁺ dependent ATPase (SERCA) inhibitor conjugated to a peptide targeting prostate-specific membrane antigen (PSMA):
*N*⁴-(12-{{(3S,3aR,4S,6S,6aR,7S,8S,9bS)-6-(acetyloxy)-3,3a-dihydroxy-3,6,9-trimethyl-8-{{(2Z)-2-methylbut-2-enoyl}oxy}-7-(octanoyloxy)-2-oxo-2,3,3a,4,5,6,6a,7,8,9b-decahydroazuleno[4,5-*b*]furan-4-yl}oxy}-12-oxododecyl)-L-asparaginyll-L-γ-glutamyl-L-γ-glutamyl-L-γ-glutamyl-L-glutamic acid

*transferrin aldifitox (95)*³³

a conjugate of the precursor of human serotransferrin (siderophillin) with a primary amine group used to form an amidine with (4-iminobutane-1,4-diyl)sulfanediyl[(3RS)-2,5-dioxopyrrolidine-1,3-diyl]-1,3-phenylenecarbonyl and forming an *N*-benzoyl derivative of a primary amine group of diphtheria [550-L-phenylalanine]toxin from *Corynebacterium diphtheriae*-(26-560)-peptide

zoptarelin doxorubicin (107)

[6-D-lysine]human gonadoliberin-1 (LHRH) and doxorubicin covalently linked together with glutaric acid:
5-oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-*N*⁶-[5-(2-{{(2S,4S)-4-[(3-amino-2,3,6-trideoxy-α-L-*lyxo*-hexopyranosyl)oxy]-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-1,2,3,4,6,11-hexahydrotetracen-2-yl}-2-oxoethoxy)-5-oxopentanoyl]-D-lysine-L-leucyl-L-arginyl-L-prolylglycinamide

³³ The names and the descriptions of toxins are published in Annex 4.1 of "International Nonproprietary Names (INN) for pharmaceutical substances. Names for radicals, groups & others: comprehensive list (WHO/EMP/RHT/TSN/2015.1)".

ANNEX 3 .

List of INN for pegylated substances

classified by groups

Aptamers, classical and mirror ones (**-apt-**)

avacincaptad pegol (113), egaptivon pegol (111), emapticap pegol (108), lexaptepid pegol (108), olaptosed pegol (109), pegaptanib (88), pegnivacogin (106)

Blood coagulation cascade inhibitors (**-cogin**)

pegnivacogin (106)

Blood coagulation factors (**-cog**)

damoctocog alfa pegol (109), eptacog alfa pegol (activated) (101), nonacog beta pegol (104), ruriococog alfa pegol (111), turoctocog alfa pegol (108)

Colony stimulating factors (CSFs) (**-stim**)

eflapgrastim (111), empegfilgrastim (107), lipegfilgrastim (107), mecapegfilgrastim (113), pegacaristim (80), pegbovigrastim (109), pegfilgrastim (86), pegnartograstim (80), pegteograstim (109)

Enzymes (**-ase**)

calaspargase pegol (105), elapegademase (116), pegademase (63), pegadricase (105), pegargiminase (111), pegaspargase (64), pegcrisantaspase (111), pegloticase (98), pegorgotein (72), pegunigalsidase alfa (115), pegvaliase (111), pegvorhialuronidase alfa (115), pegzilarginase (117)

Erythropoietin type blood factors (**-poetin**)

pegdarbepoetin beta (117)

Growth factors and tumour necrosis factors (TNF) (**-ermin**)

pegbelfermin (120)

Growth hormone (GH) derivatives (**som-**)

efpegsomatropin (115), lonapegsomatropin(118), somatropin pegol (103)

Growth hormone antagonists

pegvisomant (82)

Hirudin derivatives (**-irudin**)

pegmusirudin (77)

Insulins

insulin peglispro (107)

Interferons

cepeginterferon alfa-2b (105), mipeginterferon alfa-2b (114), peginterferon alfa-2a (84), peginterferon alfa-2b (84), peginterferon alfacon-2 (116), peginterferon beta-1a (108), peginterferon lambda-1a (105), ropeginterferon alfa-2b (109), sampeginterferon beta-1a (116)

Interleukin type substances (**-kin**)

pegaldesleukin (74), pegilodecakin (117)

Monoclonal antibodies (**-mab**)

alacizumab pegol (98), certolizumab pegol (97), dapirolizumab pegol (110), enlimomab pegol (77), lulizumab pegol (111), rivabazumab pegol (113)

Peptides and Glycopeptides (**-tide**)

efinopegdutide (118), pegapamodutide (116), peginesatide (108)

Receptor molecules, native or modified (**-cept**)

pegsunercept (95)

Others:

abicipar pegol (108), pegcetacoplan (118), pegdinetanib (103)

ANNEX 4.

Transliteration of Greek letters in English, French and Spanish

Upper case	Lower case	English	French	Spanish
A	α	alfa (and not alpha)	alfa (and not alpha)	alfa
B	β	beta	bêta	beta
Γ	γ	gamma	gamma	gamma
Δ	δ	delta	delta	delta
E	ε	epsilon	epsilon	épsilon
Z	ζ	zeta	zêta	<u>d</u>seta *
H	η	eta	êta	eta
Θ	θ	theta	thêta	<u>z</u>eta *
I	ι	iota	iota	iota
K	κ	kappa	kappa	kappa
Λ	λ	lambda	lambda	lambda
M	μ	mu	mu	mi
N	ν	nu	nu	ni
Ξ	ξ	xi	xi	xi
O	ο	omicron	omicron	ómicron
Π	π	pi	pi	pi
P	ρ	rho	rhô	ro
Σ	σ	sigma	sigma	sigma
T	τ	tau	tau	tau
Υ	υ	upsilon	upsilon	ípsilon
Φ	φ	phi	phi	fi
X	χ	chi	khi	ji
Ψ	ψ	psi	psi	psi
Ω	ω	omega	oméga	omega

* letters to be avoided

ANNEX 5 .

Previous naming schemes for monoclonal antibodies

(From Proposed INN List 103 up to Proposed INN List 117)

- INN for monoclonal antibodies (mAb) are composed of a prefix, a substem A, a substem B and a suffix.
- The common stem for mAbs is **-mab**, placed as a suffix.
- The stem **-mab** is to be used for all products containing an immunoglobulin variable domain which binds to a defined target.
- **Substem B** indicates the species on which the immunoglobulin sequence of the mAb is based (shown in Table 7).

Table 7: Substem B for the species.

-a-	rat
-axo-	rat-mouse (pre-substem)
-e-	hamster
-i-	primate
-o-	mouse
-u-	human
-vet-	veterinary use (pre-substem)
-xi-	chimeric
-xizu-	chimeric-humanized
-zu-	humanized

The distinction between chimeric and humanized antibodies is as follows:

Chimeric: A chimeric antibody is one for which both chain types are chimeric as a result of antibody engineering. A chimeric chain is a chain that contains a foreign variable domain (originating from one species other than human, or synthetic or engineered from any species including human) linked to a constant region of human origin. The variable domain of a chimeric chain has a V region amino acid sequence which, analysed as a whole, is closer to non-human species than to human.

Humanized: A humanized antibody is one for which both chain types are humanized as a result of antibody engineering. A humanized chain is typically a chain in which the complementarity determining regions (CDR) of the variable domains are foreign (originating from one species other than human, or synthetic) whereas the remainder of the chain is of human origin. Humanization assessment is based on the resulting amino acid sequence, and not on the methodology per se, which allows protocols other than grafting to be used. The variable domain of a humanized chain has a V region amino acid sequence which, analysed as a whole, is closer to human than to other species.

Note: The infix

-xizu- is used for an antibody having both chimeric and humanized chains.

-axo- is used for an antibody having both rat and mouse chains.

- **Substem A** indicates the target (molecule, cell and organ) class (shown in Table 8).

Table 8: Substem A for target class.

-b(a)-	bacterial
-am(i)-	serum amyloid protein (SAP)/amyloidosis (pre-substem)
-c(i)-	cardiovascular
-f(u)-	fungal
-gr(o)-	skeletal muscle mass related growth factors and receptors (pre-substem)
-k(i)-	interleukin
-l(i)-	immunomodulating
-n(e)-	neural
-s(o)-	bone
-tox(a)-	toxin
-t(u)-	tumour
-v(i)-	viral

In principle, a single letter, e.g. **-b-** for bacterial is used as substem A. Whenever substem B starts with a consonant (e.g. *x* or *z*), to avoid problems in pronunciation, an additional vowel indicated in the table, e.g. **-ba-** is inserted.

Prefix

The prefix should be random, i.e. the only requirement is to contribute to a euphonious and distinctive name.

Second word

If the monoclonal antibody is conjugated to another protein or to a chemical (e.g. chelator), identification of this conjugate is accomplished by use of a separate, second word or acceptable chemical designation. For instance, for mAbs conjugated to a toxin, the suffix **-tox** is used in the second word.

If the monoclonal antibody is radiolabelled, the radioisotope is listed first in the INN, e.g. *technetium (^{99m}Tc) nofetumomab merpentan (81)*.

Pegylation

For pegylated monoclonal antibodies see item 2.4: General policy for pegylated substances..

Glycosylation

For glycosylated monoclonal antibodies see item 2.9: General policy for glycosylated substances.

Previous naming scheme for monoclonal antibodies

(up to Proposed INN List 102)

- The common stem for monoclonal antibodies is *-mab*.
- Sub-stems for source of product:

<i>-a-</i>	rat
<i>-axo-</i> (<i>pre-sub-stem</i>)	rat-murine hybrid
<i>-e-</i>	hamster
<i>-i-</i>	primate
<i>-o-</i>	mouse
<i>-u-</i>	human
<i>-xi-</i>	chimeric
<i>-zu-</i>	humanized

The distinction between chimeric and humanized antibodies is as follows:

A chimeric antibody is one that contains contiguous foreign-derived amino acids comprising the entire variable region of both heavy and light chains linked to heavy and light constant regions of human origin.

A humanized antibody has segments of foreign-derived amino acids interspersed among variable region segments of human-derived amino acid residues and the humanized heavy-variable and light-variable regions are linked to heavy and light constant regions of human origin.

- Sub-stems for disease or target class:

<i>-ba(c)-</i>	bacterial
<i>-ci(r)-</i>	cardiovascular
<i>-fung-</i>	fungal
<i>-ki(n)-</i> (<i>pre-sub-stem</i>)	interleukin
<i>-le(s)-</i>	inflammatory lesions
<i>-li(m)-</i>	immunomodulator
<i>-os-</i>	bone
<i>-vi(r)-</i>	viral

tumours:

- <i>co(l)</i> -	colon
- <i>go(t)</i> -	testis
- <i>go(v)</i> -	ovary
- <i>ma(r)</i> -	mammary
- <i>me(l)</i> -	melanoma
- <i>pr(o)</i> -	prostate
- <i>tu(m)</i> -	miscellaneous

Whenever there is a problem in pronunciation, the final letter of the sub-stems for diseases or targets may be deleted, e.g. -*vi(r)*-, -*ba(c)*-, -*li(m)*-, -*co(l)*-, etc.

Prefix:

Should be random e.g. the only requirement is to contribute to a euphonious and distinctive name.

Second word:

If the product is radiolabelled or conjugated to another chemical, such as toxin, identification of this conjugate is accomplished by use of a separate, second word or acceptable chemical designation.

If the monoclonal antibody is used as a carrier for a radioisotope, the latter will be listed first in the INN, e.g. *technetium (^{99m}Tc) pintumomab (86)*.

-toxa- infix

For monoclonals conjugated to a toxin, the infix -*toxa*- can be inserted either into the first (main) name or included in the second word.

ANNEX 6.

Reference to publications containing proposed Lists of INN

List no. and reference

- 1 *Chron. Wld Hlth Org.* 7: 299 (1953)
- 2 *Chron. Wld Hlth Org.* 8: 216 (1954)
- 3 *Chron. Wld Hlth Org.* 8: 313 (1954)
- 4 *Chron. Wld Hlth Org.* 10: 28 (1956)
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- 6 *Chron. Wld Hlth Org.* 12: 102 (1958)
- 7 *WHO chronicle* 13: 105 (1959)
- 8 *WHO chronicle* 13: 152 (1959)
- 9 *WHO chronicle* 14: 168 (1960)
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- 45 *WHO chronicle* 35: No. 3, suppl. (1981)

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- 46 *WHO chronicle* 35: No. 5, suppl. (1981)
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- 49 *WHO chronicle* 37: No. 2, suppl. (1983)
- 50 *WHO chronicle* 37: No. 5, suppl. (1983)
- 51 *WHO chronicle* 38: No. 2 suppl. (1984)
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- 57 *WHO drug information* 1: No. 2 (1987)
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