

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

(a review)

2016



**World Health
Organization**

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**World Health
Organization**

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)

FORMER DOCUMENT NUMBER: INN Working Document 05.179

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Printed by the WHO Document Production Services, Geneva, Switzerland

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

As a result of the scientific and technical developments over the past few years and continuing now, new products of biotechnology and other biological products have been developed and approved for clinical use and more products can be expected for the treatment or prevention of disease. Examples include recombinant blood products, transgenic products (human proteins expressed in animals or plants), products 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 situation 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 all 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 INNs 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 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 respective 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>rsen</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>
Cell therapy products (see items 2.5 and 3.7)	- <i>cel</i>
Colony stimulating factors (see item 3.8)	- <i>stim</i>
Enzymes (see item 3.9)	- <i>ase</i>
Erythropoietin type blood factors (see item 3.10)	- <i>poetin</i>
Gene therapy products (see items 2.6 and 3.11)	- <i>gene</i>
Gonadotropin-releasing hormone (GnRH) inhibiting peptides (see item 3.12)	- <i>relix</i>
Growth factors and Tumour necrosis factors (TNF) (see item 3.13)	- <i>ermin</i>
Growth hormone (GH) derivatives (see item 3.14)	- <i>som-</i>
Heparin derivatives including low molecular mass heparins (see item 3.16)	- <i>parin</i>
Hirudin derivatives (see item 3.17)	- <i>irudin</i>
Immunomodulators, both stimulant/suppressive and stimulant (see item 3.18)	- <i>imod</i>
Interleukin receptor antagonists (see item 3.21)	- <i>kinra</i>
Interleukin type substances (see item 3.22)	- <i>kin</i>
Monoclonal antibodies (see items 2.7 and 3.23)	- <i>mab</i>
Oxytocin derivatives (see item 3.24)	- <i>tocin</i>
Peptides and glycopeptides (see item 3.25)	- <i>tide</i>
Pituitary hormone-release stimulating peptides (see item 3.26)	- <i>relin</i>
Receptor molecules, native or modified (see item 3.28)	- <i>cept</i>
Small interfering RNA (see item 3.29)	- <i>siran-</i>
Synthetic polypeptides with a corticotropin-like action (see item 3.30)	- <i>actide</i>
Vasoconstrictors, vasopressin derivatives (see item 3.33)	- <i>pressin</i>

1.2. Groups with INN schemes

Name of the group
Cell therapy products (see items 2.5 and 3.7)
Gene therapy products (see items 2.6 and 3.11)
Monoclonal antibodies (see items 2.7 and 3.23)

1.3. Groups without respective stems / pre-stems

Name of the group
Antithrombins (see item 3.3)
Growth hormone (GH) antagonists (see item 3.15)
Insulins (see item 3.19)
Interferons (see item 3.20)
Pituitary / placental glycoprotein hormones (see item 3.26)
Thrombomodulins (see item 3.31)
Toxins (see item 3.32)
Vaccine-like substances (eg. peptide vaccines, recombinant vaccines) (see items 2.12 and 3.34)

2. GENERAL POLICIES FOR BIOLOGICAL AND BIOTECHNOLOGICAL SUBSTANCES

2.1. General policies for non-glycosylated compounds [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 policies for glycosylated compounds [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));
- differences in glycosylation pattern are 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), *agglucosidase alfa* (91), *epoetin beta* (62)).

For *-mab* and *-cept*:

Although most monoclonal antibodies (*-mab*) (see items 2.7 and 3.23) and receptor molecules (*-cept*) (see item 3.28) 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 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*”.

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

2.3. General policies for fusion proteins² [4]

- INN have been assigned to some fusion proteins. If a stem exists for one or the other part of the fusion protein, this stem should be brought into the name. This allows the constant part of a fusion protein to be recognized in the name.
- At present, it is considered unnecessary to indicate that the product is a fusion product within the name, but this position may need to be reviewed in the future.
- 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 *-cept* group.

2.4. General policies 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 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 (eg. *peginterferon alfa-2b* (84), *pegfilgrastim* (86)) 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. *cepeginterferon alfa-2b* (105), *empegfilgrastim* (107)).

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

2.5. General policies for cell therapy products (CTP)

During the 61st INN Consultation in 2015, an INN-USAN-harmonized nomenclature scheme for cell therapy products (CTP) (shown in Table 1) was formally finalized and approved by the members of the INN Expert Group designated to deal with the selection of international nonproprietary names³.

² The list of INN for fusion proteins is given in ANNEX 1.

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

Table 1. Nomenclature scheme for cell therapy products (CTP)

Prefix: random	Infix1: manipulation/s ^(a)	Infix2: cell type	Suffix: “-cel”
to contribute to euphonious and distinctive name, e.g.: <i>al-</i> ; <i>bet-</i> ; <i>val-</i> ...	to specify, if appropriate, which manipulation the cells have undergone, using, when available, existing infixes for manipulation ^(b) , e.g.: <i>-gen-</i> : transduced (genetic modification) <i>-fus-</i> : fusion to a cell	to identify the primary cell type ^(c) using, when available, existing infixes for cell types, e.g.: <i>-den-</i> dendritic cells <i>-mio(b)-</i> myoblasts <i>-co(n)-</i> chondrocytes <i>-fi(b)-</i> fibroblasts <i>-ker(a)-</i> keratinocytes <i>-end(o)-</i> endothelial cells <i>-leu-</i> lymphocytes/monocytes/APC (white cells) ^(d) ... ^(e)	to name <i>all</i> CTP, with the <i>exception</i> of : - Minimally manipulated hematopoietic elements - Combination products

^(a) There may be more than one manipulation infix in the same INN.

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

^(c) Residual, contamination cells are not named.

^(d) The cell type infix *-leu-* will be used to describe hematopoietic cell preparations that do not fit a particular or specific cell type. Such cell preparations may be comprised of a mixture of the 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 the definition of dendritic cells fall into this category.

^(e) **-cor-** for *umbilical cord cells*; **-ep(a)-** for *hepatocytes*; **-isle-** for *islet cells*; **-mestro-** for *mesenchymal stromal cells (msc)*; **-ova-** for *ovary cells*; **-pla(c)-** for *placenta cells*; **-ret-** for *retinal epithelial cells*; **-ren-** for *renal tubular cells*; **-ur-** for *urothelial cells*; **-tem-** for *stem cells*; **-defitem-** for *differentiated stem cells* (not filling in any existing category); **-tesi-** for *testis cells*; **-tu-** for *tumor cells*.

Note: Information concerning manipulations and/or modifications, and the type of the CTP (i.e. allogeneic, autologous and xenogeneic) would be specified in the description of the product.

2.6. General policies for gene therapy products (GTP)[2]

In 2005, the two-word nomenclature scheme for gene therapy products was formally adopted by the members of the INN Expert Group designated to deal with the selection of nonproprietary names. The 2012 updated scheme is shown in Table 2.

Table 2: Two-word scheme for gene therapy products (GTP) (updated in 2012)

	Prefix	Infix	Suffix
word 1 (gene component)	random to contribute to euphonious and distinctive name e.g. <i>al-</i> <i>bet-</i> <i>val-</i>	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>-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	<i>-(a vowel)gene</i> e.g. <i>-(o)gene</i>
word 2 (vector component)	random to contribute to euphonious and distinctive name	e.g.: <i>-adeno-</i> adenovirus <i>-cana-</i> canarypox virus <i>-foli-</i> fowlpox virus <i>-herpa-</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)
			<i>-plasmid</i> (plasmid vector)

In the case of non-plasmid DNA GTP, there is no need for a second word in the name.

2.7. General policies for monoclonal antibodies [1, 3, 11, 23]⁴

- 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 3).

Table 3. 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
-xi <u>z</u> u-	chimeric-humanized
- <u>z</u> u-	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

⁴ It contains the revised naming scheme for monoclonal antibodies; the previous naming scheme for monoclonal antibodies is given in ANNEX 5.

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 4).

Table 4. 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 policies for pegylated substances [22].

Glycoylation

For glycosylated monoclonal antibodies see item 2.7: General policies for glycosylated compounds [8].

2.8. General policies for blood products [4]

- INN have not been assigned to natural human blood products.
- Many natural blood products have well-established names, so 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.

2.9. General policies for immunoglobulins fractionated from plasma [9, 10]

- Not to select an INN for immunoglobulins fractionated from plasma is the current policy.
- 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.

2.10. General policies for skin substitutes [4]

The products within this system are made of cells within a matrix, and skin substitutes can be considered to be engineered tissue and thus fall outside the scope of the INN system.

2.11. General policies for transgenic substances [4] (*under discussion*)

- 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)).

2.12. General policies for vaccines [4-7] (*under discussion*)

- 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 vaccines⁵ (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 disease, 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 monograph.
- During the INN Consultation in 1993, it was agreed that the prerequisite for an INN application for a recombinant vaccine⁶ 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]).

⁵ The definition of peptide vaccines is given in item 3.34.

⁶ The definition of recombinant vaccines is given in item 3.34.

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)⁷, *omiganan* (89), *pexiganan* (78).

3.2. Antisense oligonucleotides⁸

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

aganirsen (103), *alicaforsen* (97), *anivamersen* (105), *apatorsen* (110), *aprinocarsen* (97), *beclanorsen* (101), *cenersen* (97), *custirsen* (99), *drisapersen* (106), *eteplirsen* (103), *gataparsen* (103), *nusinersen* (112), *mipomersen* (100), *mongersen* (111), *oblimersen* (97), *prexigebersen* (114), *trabedersen* (98), *volanesorsen* (113).

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

afovirsen (97), *fomivirsen* (97), *miravirsen* (101), *radavirsen* (106), *trecovirsen* (97).

3.3. Antithrombins

antithrombin III (60), *antithrombin alfa* (93) (Rec. Glycoprotein, 432aa, from transgenic goats), *antithrombin gamma* (107).

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), *olapteted pegol* (109), *pegaptanib* (88)

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

pegnivacogin (106)

⁷ The numbers in parentheses indicate the Proposed list number.

⁸ For small interfering RNA see item 3.29 and for various see item 3.35.

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 up 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 policies for glycosylated compounds [8]).
- 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 (98), damoctocog alfa pegol (109), efmoroctocog alfa (111), lonoctocog alfa (111), moroctocog alfa (72), octocog alfa (73), rurioctocog alfa pegol (111), simoctocog alfa (104), susoctocog alfa (112), turoctocog alfa (108), turoctocog alfa pegol (108)

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

albutrepenonacog alfa (109), 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)

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

vonicog alfa (102)

3.7. Cell therapy products (CTP)

For General policies for cell therapy products (CTP) see item 2.5.

spanlecorthemlocel (112)

consists of human expanded CD34+ haematopoietic stem cells that have been isolated from umbilical cord blood and cultured in vitro in media supplemented with THPO (thrombopoietin), KITLG (KIT ligand, stem cell factor, SCF), IL6 (interleukin 6), FLT3LG (fms-related tyrosine kinase 3 (FLT3) ligand), and an antagonist of AHR (aryl hydrocarbon receptor); typically contains >10% of cells expressing CD34. (*hematopoietic stem cell transplantation*)

3.8. 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))⁹,
romiplostim (97) (platelet stimulating factor (through thrombopoietin receptor(Mpl)))¹⁰*

-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 (111), empegfilgrastim (107), filgrastim (64),
lenograstim (64), lipegfilgrastim (107), mecapegfilgrastim (113), 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).

⁹ Also known as thrombopoietin.

¹⁰ A thrombopoietin mimetic.

3.9. Enzymes

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

Enzymes are classified according to the E.C. number, i.e the reaction they catalyse¹¹.

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)
- **-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)
- 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)

¹¹ For enzyme classification and nomenclature see:

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

- EC 3.1.21.1 Deoxyribonuclease I:
-**dornase** for deoxyribonuclease (*suffix*)
dornase alfa (70), *streptodornase* (6)
- EC 3.1.27.5 Pancreatic ribonuclease
ranpirnase (81)
- EC 3.2.1.20 α -Glucosidase
alglucosidase alfa (91), *reveglucosidase alfa* (111)
- EC 3.2.1.22 α -Galactosidase
agalsidase alfa (84), *agalsidase beta* (84)
- 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 3.2.1.35 Hyaluronoglucosaminidase
bovhyaluronidase azoximer (112), *hyalosidase* (50), *hyaluronidase* (1),
vorhyaluronidase alfa (111)
- EC 3.2.1.45 Glucosylceramidase:
-**glucerase** for glucosylceramidase (*suffix*)
alglucerase (68), *imiglucerase* (72), *taliglucerase alfa* (101), *velaglucerase alfa* (98)
- EC 3.2.1.76 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), duteplase (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 in a fusion protein
amediplase (79)
- EC 3.4.24.72 Fibrolase
alfimeprase (85), brinase (22), ocrase (28)
- 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)
- EC 3.5.3.6 Arginine deiminase
pegargiminase (111)
- EC 3.5.4.4 Adenosine deaminase
pegademase (63)
- **-liase** for lyase (decarboxylase) (*suffix*):
EC 4.2.2.20 Chondroitin-sulfate-ABC endolyase
condoliase (106)

EC 4.3.1.24 Phenylalanine ammonia-lyase

pegvaliase (111)

- Exceptions, without **-ase** suffix:

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), sultilains (18)(EC 3.4.21.62)

- Co-enzymes:

cobamamide (15)(!), cocarboxylase (1), mecobalamin (26) (!), streptokinase (6), ubidecarenone (48)

3.10.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 compounds of the same amino acid sequence as human erythropoietin which vary in the glycosylation pattern (see item 2.2: General policies for glycosylated compounds [8]).

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

darbepoetin alfa (85), 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).

3.11.Gene therapy products

For General policies for gene therapy products (GTP)[2] see item 2.6.

aglatimagene besadenovec (113), alferminogene tadenovec (95), alipogene tiparvovec (99), amolimogene bepiplasmid (98), axalimogene filolisbac (112), beperminogene perplasmid (95), contusogene ladenovec (97), golnerminogene pradenovec (101), lenadogene nolparvovec (114), mesmulogene ancovacivec (114), pexastimogene devacirepvec (108), riferminogene pecaplasmid (100), rilimogene galvacirepvec (107), rilimogene glafolivec (107), sitimagene ceradenovec (97), taberminogene vadenovec (100), talimogene laherparepvec (104), tipapkinogene sovacivec (102), velimogene aliplasmid (97), vocimagene amiretrorepvec (107).

3.12. 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), *itirelix* (79), *ozarelix* (94), *prazarelix* (81), *ramorelix* (69), *teverelix* (78).

3.13. Growth factors and Tumour Necrosis Factors (TNF)

The common stem for growth 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:

ersofermin (66), *palifermin* (88), *repifermin* (82), *sprifermin* (105), *trafermin* (74), *velafermin* (94)

-filermin for leukaemia-inhibiting factors:

emfilermin (82)

-nermin for tumour necrosis factors:

ardenermin (88), *dulanermin* (99), *plusonermin* (73), *sonermin* (68), *tasonermin* (78)

-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:

cimaglermin alfa (110) (recombinant DNA derived glial growth factor 2 (GGF2))
dapiclermin (93) (modified ciliary neurotrophic factor (CNTF)).

3.14. Growth hormone (GH) derivatives

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

Human growth hormone derivatives:

albusomatropin (114), *efpegssomatropin* (113), *somapacitan* (112), *somatrem* (54),
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 3.27)
somatostatin (46) (growth hormone release inhibitor).

3.15. Growth hormone (GH) antagonists

pegvisomant (82)

3.16. Heparin derivatives including low molecular mass heparins

The common stem for heparin derivatives including low molecular mass 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).

3.17. Hirudin derivatives

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

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

3.18. Immunomodulators, both stimulant/suppressive and stimulant (*under discussion*)

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)

leftolimod (113) (DNA based immunomodulator agent)

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

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

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

Others:

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

3.19. Insulins

Up to now, the insulin derivatives have been named using the two-word approach. The compounds 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).

3.20. 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, or in the case of mixtures, by additional codes. Additional Arabic numbers can be 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 beta-1a* (108), *peginterferon lambda-1a* (105), *ropeginterferon alfa-2b* (109).

3.21. 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)

3.22. 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 compounds [8].

-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), *celmoleukin* (65), *denileukin diftitox* (78),
pegaldesleukin (74), *teceleukin* (67), *tucotuzumab celmoleukin* (95)

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

binetrakin (82)

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

atexakin alfa (72)

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

canoctakin (110), *emoctakin* (74)

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

ilodecakin (81)

-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

daniplestim (76), *muplestim* (74)

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

abrineurin (84).

3.23. Monoclonal antibodies

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

For General policies for monoclonal antibodies [1, 3, 11, 23] see item 2.7.

For glycosylated monoclonal antibodies see item 2.2: General policies for glycosylated compounds [8].

INN for monoclonal antibodies alphabetically ordered by substem B (for the species) and by substem A (for the target class):

-axomab (pre-substem, rat-murine hybrid):

catumaxomab (93), *ertumaxomab* (93)

-omab (mouse):

-b(a)- (bacterial, under the previous naming scheme *-ba(c)-*):

edobacomab (80)

-c(i)- (cardiovascular, under the previous naming scheme *-ci(r)-*):

biciromab (66), *imciromab* (66)

-l(i)- (immunomodulating, under the previous naming scheme *-li(m)-*):

afelimomab (80), *begelimomab* (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)

-t(u)- (tumour, under the previous naming scheme *-tu(m)-* ; *-co(l)-* ; *-go(t)-* ; *-go(v)-* ; *-ma(r)-* ; *-me(l)-* ; *pr(o)-*):

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 paptox* (84), *technetium (^{99m}Tc)*

nofetumomab merpentan (81), *technetium* (^{99m}Tc) *pintumomab* (86), *tenatumomab* (99), *tositumomab* (80)

Other (infix no longer formally acknowledged under the revised scheme):

-le(s)- (inflammatory lesions):

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

-umab (human):

-b(a)- (bacterial, under the previous naming scheme *-ba(c)-*):

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

-c(i)- (cardiovascular, under the previous naming scheme *-ci(r)-*):

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

-f(u)- (fungal, under the previous naming scheme *-fung-*):

efungumab (95)

-gr(o)- (skeletal muscle mass related growth factors and receptors (pre-substem)):

bimagrumab (111), *trevogrumab* (113)

-k(i)- (interleukin, under the previous naming scheme *-ki(n)-*):

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

-l(i)- (immunomodulating, under the previous naming scheme *-li(m)-*):

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

-n(e)- (neural, under the previous naming scheme *-ne(r)-*):

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

-s(o)- (bone, under the previous naming scheme *-os-*):

denosumab (94)

-tox(a)- (toxin):

actoxumab (111), *bezlotoxumab* (107), *tosatoxumab* (109)

-t(u)- (tumour, under the previous naming scheme *-tu(m)-* ; *-co(l)-* ; *-go(t)-* ; *-go(v)-* ; *-ma(r)-* ; *-me(l)-* ; *pr(o)-*):

adecatumumab (90), *anetumab ravtansine* (109), *cixutumumab* (100), *conatumumab* (99), *daratumumab* (101), *drozitumab* (103), *dusigitumab* (108), *elgentumab* (112), *enfortumab vedotin* (109), *figitumumab* (100), *flanvotumab* (106), *ganitumab* (103), *glembatumumab* (102), *glembatumumab vedotin* (113), *indusatumab* (112), *indusatumab vedotin* (112), *intetumumab* (101), *iratumumab* (94), *lexatumumab* (95), *lucatumumab* (98), *mapatumumab* (93), *narnatumab* (105), *necitumumab* (100), *ofatumumab* (93), *olaratumab* (103), *panitumumab* (96), *patritumab* (106), *pritumumab* (89), *radretumab* (104), *rilotumumab* (101), *robatumumab* (100), *seribantumab* (108), *tarextumab* (109), *teprotumumab* (108), *tisotumab* (113), *tisotumab vedotin* (113), *tovetumab* (109), *vantictumab* (109), *votumumab* (80), *zalutumumab* (93)

-v(i)- (viral, under the previous naming scheme *-vi(r)-*):

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

Others:

crotedumab (114) (treatment of diabetes)
roledumab (103), (treatment of RhD(+) incompatible transfusions)

-vetmab (veterinary use):

blontuvmab (114), *lokivetmab* (112), *tamtuvmab* (114)

-ximab (chimeric):

-b(a)- (bacterial, under the previous naming scheme *-ba(c)-*):

pagibaximab (93)

-c(i)- (cardiovascular, under the previous naming scheme *-ci(r)-*):

abciximab (80), *volociximab* (93)

-l(i)- (immunomodulating, under the previous naming scheme *-li(m)-*):

basiliximab (81), *clenoliximab* (77), *galiximab* (89), *infliximab* (77), *keliximab* (81), *lumiliximab* (90), *priliximab* (80), *teneliximab* (87), *vapaliximab* (87)

-tox(a)- (toxin):

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

-t(u)- (tumour, under the previous naming scheme *-tu(m)-* ; *-co(l)-* ; *-go(t)-* ; *-go(v)-* ; *-ma(r)-* ; *-me(l)-* ; *pr(o)-*):

amatuximab (104), *bavituximab* (95), *brentuximab vedotin* (103), *carotuximab* (114), *cetuximab* (82), *coltuximab ravtansine* (109), *dinutuximab* (109), *dinutuximab beta* (113), *ecromeximab* (87), *ensituximab* (103), *futuximab* (107), *girentuximab* (101), *indatuximab ravtansine* (105), *iodine (¹³¹I) derlotuximab biotin* (113), *iodine (¹²⁴I) 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), *ublutuximab* (104), *vadastuximab* (114), *vadastuximab talirine* (113)

-xizumab (chimeric-humanized):

navicixizumab (114)¹², *ontuxizumab* (109), *otelixizumab* (99), *pasotuxizumab* (111)

-zumab (humanized):

-b(a)- (bacterial, under the previous naming scheme *-ba(c)-*):

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

-c(i)- (cardiovascular, under the previous naming scheme *-ci(r)-*):

alacizumab pegol (98), *bevacizumab* (86), *bevacizumab beta* (114), *bococizumab* (110), *brolocizumab* (112), *caplacizumab* (106), *concizumab* (108), *demcizumab* (107), *emicizumab* (113), *etaracizumab* (99), *idarucizumab* (109), *lodelcizumab* (108), *ralpancizumab* (110), *tadocizumab* (94), *vanucizumab* (113)¹²

-gr(o)- (skeletal muscle mass related growth factors and receptors (pre-substem)):

domagrozumab (114), *landogrozumab* (113)

-k(i)- (interleukin, under the previous naming scheme *-ki(n)-*):

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

-l(i)- (immunomodulating, under the previous naming scheme *-li(m)-*):

apolizumab (87), *aselizumab* (88), *atezolizumab* (112), *benralizumab* (102), *cabiralizumab* (114), *cedelizumab* (81), *certolizumab pegol* (97), *daclizumab* (78), *daclizumab beta* (114), *dapirolizumab pegol* (110), *eculizumab* (87), *efalizumab* (85), *erlizumab* (84), *etrolizumab* (104), *fontolizumab* (87), *ibalizumab* (97), *inebilizumab*

¹² bi-specific monoclonal antibody.

(113), itolizumab (103), lampalizumab (107), lendalizumab (114), ligelizumab (107), lulizumab pegol (111), mepolizumab (81), mogamulizumab (104), monalizumab (113), natalizumab (79), nemolizumab (112), ocrelizumab (95), omalizumab (84), ozoralizumab (105), pascolizumab (87), pateclizumab (105), pembrolizumab (110), pexelizumab (86), pidilizumab (108), plozalizumab (113), pogalizumab (114), quilizumab (106), reslizumab (85), rontalizumab (101), rovelizumab (81), ruplizumab (83), samalizumab (105), sapelizumab (114), sipilizumab (87), talizumab (89), teplizumab (97), tocilizumab (90), toralizumab (87), tregalizumab (104), vatelizumab (105), vedolizumab (100), visilizumab (84), vobarilizumab (114)¹²

-n(e)- (neural, under the previous naming scheme -ne(r)-):

bapineuzumab (93), crenezumab (105), galcanezumab(114)¹², ozanezumab (108), ponezumab (104), refanezumab (114), solanezumab (107), tanezumab (99)

-s(o)- (bone, under the previous naming scheme -os-):

blosozumab (105), romosozumab (106)

-tox(a)- (toxin):

urtoxazumab (90)

-t(u)- (tumour, under the previous naming scheme -tu(m)- ; -co(l)- ; -go(t)- ; -go(v)- ; -ma(r)- ; -me(l)- ; pr(o)-):

abitudumab (109), alemtuzumab (83), bivatumab (86), brontictuzumab (111), cantuzumab mertansine (105), cantuzumab ravtansine (105), cergutuzumab amunaleukin (113), citatumab bogatox (99), clivatuzumab tetraxetan (113), codrituzumab (109), dacetuzumab (98), dalotuzumab (107), denintuzumab mafodotin (111), duligotuzumab (110), elotuzumab (100), emactuzumab (111), emibetuzumab (111), enavatuzumab (104), enoblituzumab (114), epratuzumab (82), farletuzumab (100), fibatumab (113), ficlatuzumab (105), gemtuzumab (83), imgatumab (107), inotuzumab ozogamicin (92), labetuzumab (85), labetuzumab govitecan (113), lifastuzumab vedotin (110), lintuzumab (86), lorvotuzumab mertansine (103), lumretuzumab (111), matuzumab (88), milatumab (98), nimotuzumab (94), obinutuzumab (109), ocaratuzumab (107), onartuzumab (104), oportuzumab monatox (100), otlertuzumab (110), parsatumab (107), pertuzumab (89), pinatumab vedotin (108), polatumab vedotin (110), rovalpituzumab (113), rovalpituzumab tesirine (113), sacituzumab govitecan (113), sibrotuzumab (86), simtuzumab (107), sofituzumab vedotin (110), sontuzumab (94), tigatumab (98), trastuzumab (78), trastuzumab emtansine (103), tucotuzumab celmoleukin (95), vandortuzumab vedotin (112), veltuzumab (98), vorsetuzumab (107), vorsetuzumab mafodotin (107), xentuzumab (114)¹², yttrium (⁹⁰Y) clivatuzumab tetraxetan (102), yttrium ⁹⁰Y tacatumab tetraxetan (93)A

-v(i)- (viral, under the previous naming scheme -vi(r)-):

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

Other:

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

Other:

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)

3.24.Oxytocin derivatives

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

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

3.25.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 3.30), **-pressin** (Vasoconstrictors, vasopressin derivatives, item 3.33), **-relin** (Pituitary hormone-release stimulating peptides, item 3.27), **-tocin** (Oxytocin derivatives, item 3.24)

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), *dulaglutide* (103), *elsiglutide* (104), *liraglutide* (87), *semaglutide* (101), *tasoglutide* (99), *teduglutide* (90)

-motide for peptides used as immunological agents for active immunization:

abecomotide (109), *alicdamotide* (109), *amilomotide* (105), *asudemotide* (107), *disomotide* (94), *elpamotide* (103), *graunimotide* (113), *latromotide* (107), *ovemotide* (94), *pradimotide* (107), *tanurmotide* (109), *tecemotide* (108), *tertomotide* (98), *tiplimotide* (82), *trempamotide* (107), *zastumotide* (110)

-ritide for natriuretic peptides:

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

-fiba- for platelet aggregation inhibitor (GPIIb/IIIa receptor antagonist):

eptifibatide (78) (antithrombotic)

-melano- for melanocortin receptor agonists:

afamelanotide (99), *bremelanotide* (95), *modimelanotide* (111), *setmelanotide* (112)

analgesic:

cibinetide (114), leconotide (86), ziconotide (78)

antiarrhythmic:

danegaptide (101), rotigaptide (94)

anti-inflammatory:

dusquetide (113), icrocaptide (89),

antidiabetic:

*albenatide (111), amlintide (76), davalintide (101), exenatide (89), langlenatide (111),
lixisenatide (99), pramlintide (74), seglitide (57)*

antineoplastic:

paclitaxel trevatide (109), satoreotide trizoxetan (114)

antiviral:

enfuvirtide (85), tifuvirtide (91)

autoimmune disorders:

dalazatide (111), dirucotide (100)

cicatrisation promoter:

aclerastide (110), ensereptide (107)

diagnostic:

*betiatide (58), bibapcitide (78), ceruletide (34), depreotide (80), flotegatide (¹⁸F) (108),
fluciclatide (¹⁸F) (103), maraciclatide (103), mertiatide (60), pendetide (70), technetium
(^{99m}Tc) apcitide (86), technetium (^{99m}Tc) etarfolatide (107), teriparatide (50)*

gastro-intestinal bleeding / antineoplastic:

*edotreotide (84), ilatreotide (68), lanreotide (64), octreotide (52), pentetreotide (66),
vapeotide (62)*

gastro-intestinal functions normalizing agents:

dolcanatide (114), linaclotide (97), plecanatide (104)

hormone analogues:

abaloparatide (109), semparatide (80), teriparatide (50) (see category “diagnostic”)

immunological agents (antineoplastics):

*almurtide (74), delmitide (92), edratide (89), goralatide (72), mifamurtide (95),
murabutide (49), pentigetide (60), pimelautide (53), prezatide copper acetate (67),
rolipoltide (94), romurtide (61), tabilautide (60), temurtide (60), tigapotide (95)*

neuromodulator / neuroprotective agents:

davunetide (100), *ebiratide (56)*, *obinepitide (96)*, *trofinetide (112)*, *vanutide cridificar (100)*

peptic ulcer:

sulglycotide (29), *triletide (50)*

pulmonary surfactants:

lusupultide (80), *sinapultide (78)*

treatment of Parkinson's disease:

doreptide (59), *pareptide (38)*

Others:

balixafortide (112) (chemokine CXCR4 receptor antagonist)

brimapitide (114) (selective target and inhibitor of c-Jun-N-terminal kinases (JNKs))

cilengitide (81) (angiogenesis inhibitor)

disiteritide (99) (transforming growth factor beta-1 inhibitor)

ecallantide (93) (kallikrein inhibitor)

elamipretide (113) (cardiolipin peroxidase inhibitor)

emideltide (70) (sedative)

etelcalcetide (112) (calcium sensing receptor agonist)

fexapotide (114) (apoptosis inducer)

lagatide (75) (antidiarrhoeal)

lancovutide (99) (expectorant in cystic fibrosis)

larazotide (99) (zonulin antagonist in celiac disease)

mibenratide (111) (β 1-adrenergic receptor analogue)

nemifitide (87) (antidepressant)

nosiheptide (35) (veterinary growth stimulant)

ociltide (52) (gut motility increasing)

pasireotide (90) (inhibition of growth hormone release)

peginesatide (108) (antianaemic)

rusalatide (96) (thrombin receptor as an agonist, promoter of bone and skin wound healing)

solnatide (113) (sodium channel activator)

teprotide (36) (angiotensin-converting enzyme inhibitor)

3.26.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 policies for glycosylated compounds [8]).

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

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

-gonadotropin (gonadotropin):

chorionic gonadotrophin (01) (chorionic gonadotropins, obtained from human serum and urine during pregnancy and has both lutropin and follitropin activity)

choriogonadotropin alfa (76) (human chorionic gonadotropin, glycoform alfa)

serum gonadotrophin (01) (used for the follicle stimulating hormone (FSH, follitropin) from serum of pregnant mares)

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

lutropin alfa (71)

3.27.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:

corticoirelin (66) (diagnostic agent)

3.28.Receptor molecules, native or modified (*under discussion*)

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

A preceding infix should designate the receptor type.

For glycosylated receptor molecules, native or modified see item 2.2: General policies for glycosylated compounds [8].

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

*briobacept (98)*¹³

-ber- (vascular endothelial growth factor receptors):

*aflibercept (96)*¹³, *conbercept (105)*¹³

-co- (complement receptors):

mirococept (91)

-far- (subgroup of interferon receptors):

bifarcept (86)

-fri- (frizzled family receptors):

*ipafricept (109)*¹³

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

*alefacept (84)*¹³

-na- (interleukin-1 receptors):

*rilonacept (95)*¹³

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

*asunercept (114)*¹³, *baminercept (99)*¹³, *etanercept (81)*¹³, *lenercept (72)*¹³, *onercept (86)*,
pegsunercept (95)

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

*abatacept (91)*¹³, *belatacept (93)*¹³

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

*atacicept (95)*¹³

¹³ Fc-fusion receptor molecules or membrane ligands, native or modified.

-ter- (transforming growth factor receptors):

dalantercept (105)¹³, luspatercept (110)¹³, ramatercept (108)¹³, sotatercept (104)¹³

-vir- (antiviral receptors):

alvircept sudotox (69)

3.29.Small interfering RNA¹⁴

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

asvasiran (111), bamosiran (106), bevasiranib (108), cemdisiran (114), fitusiran (113), givosiran (114), inclisiran (114), patisiran, (109), revusiran (111)

3.30.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)

3.31.Thrombomodulins

sothrombomodulin alfa (101), thrombomodulin alfa (94)

3.32.Toxins

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

3.33.Vasoconstrictors, vasopressin derivatives

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

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

¹⁴ For antisense oligonucleotides see item 3.2 and for various see item 3.35.

3.34. 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 as immunological agents for active immunization: **-motide** (see item 3.25).
- 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 as immunological agents 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)*)))

3.35. Various¹⁵

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-dioxoandroster-4-en-7 α -yl)thio]propionic acid, serum albumin conjugate)

Hemoglobin-based substances:

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

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

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-hexacarbaldehyde] 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*)

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

¹⁵ The descriptions following the INN names may not be the complete definitions as shown in the publications of INN Lists.

secretin human (106) (human peptide hormone secretin)

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

Nucleotide-based substances¹⁶:

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

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”)

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

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)

iropilact (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)

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))

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))

¹⁶ For antisense oligonucleotides see item 3.2, for aptamers see item 3.4 and for small interfering RNA see item 3.29.

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)-lysyl-dialanyl-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))

alisorivir (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)

enadenotucirev (111) (chimeric oncolytic adenovirus Ad3/Ad11p containing two deletions in the viral genome in the E3 region (2444 bp) and in the E4 region (24bp) and 197 non-homologous nucleotides in the E2B region)

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

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

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.

REFERENCES

1. The use of stems in the selection of International Nonproprietary Names (INN) for pharmaceutical substances, 2013, *WHO/EMP/RHT/TSN/2013.1* *
2. International nomenclature and gene therapy products (*WHO Drug Information*, Vol.19, N°2, 2005, p.103) *
3. Pre-stems:Suffixes used in the selection of INN (document regularly updated on the INN website) *
4. Consultation on International Nonproprietary Names (INN) and biological products, *INN Working Document 00.118* (2002)
5. INNs for biotechnological products: collaboration with other parties, *WHO/Pharm S/Nom 1763* (1999)
6. INNs for recombinant vaccines and viruses, *WHO/Pharm S/Nom 1719* (1998)
7. INNs for biosynthetic vaccines, *WHO/Pharm S/Nom 1419* (1994)
8. INN nomenclature for peptides, glycopeptides, proteins and glycoproteins, *WHO/Pharm S/Nom 1428* (1994)
9. INNs for immunoglobulins, *WHO/Pharm S/Nom 1517* (1995)
10. INNs for immunoglobulins, *WHO/Pharm S/Nom 101* (1967)
11. General policies for monoclonal antibodies, *INN Working Document 09.251*, 24/06/2009*
12. Definition of INNs for substances prepared by biotechnology, *WHO/Pharm S/Nom 1348* (1992)
13. International Nonproprietary Names (INN) for pharmaceutical substances, Lists 1-113 of proposed INN and Lists 1-72 of Recommended INN, Cumulative List N°15, 2013
14. Guidelines on the use of International Nonproprietary Names (INNs) for pharmaceutical substances, *WHO/Pharm S/Nom 1570* (1997)
15. INNs of the *-tropin (trophin)* series: pituitary hormones, *WHO/Pharm S/Nom 1406* (1993-1995)
16. INNs for blood factors, *WHO/Pharm S/Nom 1362* (1994)
17. INNs for growth factor, *WHO/Pharm S/Nom 1318* (1991)
18. INNs for heparin derivatives, *WHO/Pharm S/Nom 1031* (1985-1991)
19. Nomenclature of insulin injections, *WHO/Pharm S/Nom 1127* (1986)

20. Generic names for genetically-engineered insulins, *WHO/Pharm S/Nom 737 (1980-1983)*
21. International nonproprietary names (INN) for pharmaceutical substances: names for radicals, groups & others (Comprehensive list), *WHO/EMP/RHT/TSN/2015.1**
22. Conjugated substances, *INN Working Document 15.369, 01/04/2015*
23. International Nonproprietary Names (INN) Working Group Meeting on Nomenclature for MonoclonalAntibodies (mAb), *INN Working Document 08.242 (6-7/10/2008)**

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

ANNEX 1 .

The list of INN for fusion proteins^{17, 18}

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-[(23S)-23-{[exendin-4 *Heloderma suspectum* precursor-(48-86)-peptidyl (exenatidyl)]amino}-3,12,24-trioxo-7,10-dioxo-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

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)

¹⁷ Two or more proteins encoded by a single gene that possibly include a linker, where the final product is translated as a recombinant single product.

¹⁸ It should be noted that this list may not be comprehensive. The descriptions under the names are the published ones.

-ase

*asfotase alfa (104)*¹⁹

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

reveluglucosidase 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

-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 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-C_H2-C_H3 γ1-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 (γ1-chain Fc fragment), (92-92':95-95')-bisdisulfide dimer

¹⁹ INN selected before the implementation of the *ef*- suffix.

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 $\gamma 1$ 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 $\gamma 1$ -chain Fc fragment), dimer

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 \rightarrow 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

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

-cept & -tox²⁰ (-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)

-kin & -tox²⁰

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)

²⁰ 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)".

-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 & -tox²¹ (-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)

citatumumab 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

²¹ 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)".

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

nacolumab 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)

-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)²²

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

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

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)]exendin-4 *Heloderma suspectum* (Gila monster), human immunoglobulin G4 Fc fragment-(9'-229')-peptide dimer (11'-11'')-disulfide

vanutide cridificar (100)²³

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

-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-1H-pyrrole-1-yl)-N-{6-[(2,5-dioxopyrrolidin-1-yl)oxy]-6-oxohexyl}propanamide

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

²² INN selected before the implementation of the *ef*- suffix.

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)".

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^{α.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, pluripointin) (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)²⁴

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)²⁴

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-

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

valyl-L-leucyl-L-phenylalanyl-L-glutaminylglycyl-L-prolyl-L-serylglycyl-L-lysyl-L-leucyl-human annexin A5

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

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 glycylglycine plus 12 dodecapeptides of 4 different sequences of AE2G2P2S3T2

topsalsin (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)²⁵

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

trebananib (106)²⁵

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

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*).

²⁵ INN selected before the implementation of the *ef*- suffix.

ANNEX 2.

List of INN for conjugated proteins²⁶

classified by groups

-tide & -xetan

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-cysteinyl-4-[(4*S*)-2,6-dioxo-1,3-diazinane-4-carboxamido]-L-phenylalanyl-4-(carbamoylamino)-D-phenylalanyl-L-lysyl-L-threonyl-L-cysteinyl-D-tyrosinamide]

trizoxetan

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

-mab & 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)²⁷

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

-mab & tesirine

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 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-1⁵,9⁵,10,15,18,21,49,52²,52⁵-nona-oxo-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-undeca-oxa-14,17,20,48-tetraaza-1(8),9(8,10)-

²⁶ Two or more entities that are linked together by a chemical reaction *in vitro* after they have been separately produced.

²⁷ Recommended list number.

bis(pyrrolo[2,1-*c*][1,4]benzodiazepina)-52(1)-pyrrolidina-13(1,4)benzenadopentacontaphan-52³-yl

-mab & -dotin²⁸

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 maleimidecaproyl-valyl-citrullinyl-*p*-aminobenzylcarbamate (mc-val-cit-PABC) 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 maleimidecaproyl-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

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') -

²⁸ 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)".

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*-aminobenzoyloxycarbonyl (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*-aminobenzoyloxycarbonyl (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 maleimidecaproyl-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*-aminobenzoyloxycarbonyl (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 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")-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

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")-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

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

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

-mab & -xetan (for chelating agent)²⁹

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 (N^o of lysines) are substituted;

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

-mab & govitecan

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*R*S)-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)carbamoethyl]-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]carbamoethyl)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

²⁹ 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)".

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 & talirine

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

talirine

$S^{239}, S^{239''}$ -bis[(2^{11a}S,8^{11a}S,12S,15S,23³RS)-1⁴,2⁷,8⁷-trimethoxy-12-methyl-2⁵,8⁵,11,14,17,23²,23⁵-hepta-oxo-15-(propan-2-yl)-2⁵,2^{11a},8⁵,8^{11a}-tetrahydro-2¹H,8¹H-3,7-dioxo-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]

-mab & -tansine³⁰

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%) -

³⁰ 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)".

(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](methylamino)-2-methyl-5-oxopentan-2-yl)disulfanyl]-2-sulfobutanoyl

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 (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

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

Others:

mipsagargin (110)

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

*transferrin aldifitox (95)*³¹

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[(3*RS*)-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-{(2*S*,4*S*)-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

³¹ 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**)

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

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

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

Enzymes (**-ase**)

pegadricase (105), pegloticase (98), pegorgotein (72) calaspargase pegol (105), pegaspargase (64), pegcrisantaspase (111), pegargiminase (111), pegademase (63), pegvaliase (111)

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

efpegsomatropin (113), 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 beta-1a (108), peginterferon lambda-1a (105), ropeginterferon alfa-2b (109)

Interleukin type substances (**-kin**)

pegaldesleukin (74)

Monoclonal antibodies (**-mab**)

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

Peptides and Glycopeptides (**-tide**)

peginesatide (108)

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

pegsunercept (95)

Others:

pegdinetanib (103), abicipar pegol (108)

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	\omicron	omicron	omicron	ómicron
Π	π	pi	pi	pi
P	ρ	rho	rhô	ro
Σ	σ	sigma	sigma	sigma
T	τ	tau	tau	tau
Y	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 .

The previous naming scheme for monoclonal antibodies

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

<i>a</i>	rat
<i>axo (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)- (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.

