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Addendum[1] to *"The use of stems in the selection of International Nonproprietary Names (INN) for pharmaceutical substances"* WHO/EMP/RHT/TSN/2018.1

Programme on International Nonproprietary Names (INN)

Health Products Policy and Standards (HPS)
Access to Medicines and Health Products (MHP)

World Health Organization, Geneva

Addendum* to "The use of stem s in the selection of International Nonproprietary Names (INN) for pharmaceutical substances" - WHO/EMP/RHT/TSN/2018.1

* This addendum is a cumulative list of all new stems selected by the INN Expert Group since the publication of *"The use of stems in the selection of International Nonproprietary Names (INN) for pharmaceutical substances"* 2018.

-adenant	**adenosine receptors antagonists** ciforadenant (118), etrumadenant (124), inupadenant (123), preladenant (99), sipagladenant (127), taminadenant (120), tozadenant (106), vipadenant (103)
-bep	**engineered or synthetic scaffold proteins, non-immunoglobulin variable domain derived** dazodalibep (123), elarekibep (126), ensovibep (124), izokibep (122), lerodalcibep (123), palsucibep pegol (126), taldefgrobep alfa (121), tezatabep matraxetan (122), tifalibep (122) Under (c) category: abicipar pegol (108)
-bactam ***-borbactam***	β-lactamase inhibitors **β-lactamase inhibitors, boronic acid derivatives** ledaborbactam (125), ledaborbactam etzadroxil (125), taniborbactam (119), vaborbactam (113), xeruborbactam (125)
-bresib	**inhibitors of the bromodomain and extra-terminal motif (BET) family of bromodomain (BRD) proteins, antineoplastics** alobresib (117), amredobresib (126), birabresib (115), mivebresib (115), molibresib (116), pelabresib (123), trotabresib (125)
-caftor	**cystic fibrosis transmembrane regulator (CFTR) protein modulators, correctors, and amplifiers** bamocaftor (121), deutivacaftor (118), dirocaftor (123), elexacaftor (121), galicaftor (119), icenticaftor (122), ivacaftor (104), lumacaftor (105), navocaftor (121), nesolicaftor (122), olacaftor (119), posenacaftor (122), tezacaftor (114), vanzacaftor (126), zatonacaftor (128)
-calcet/-calcet-	**calcium-sensing receptors (CaSR) agonists** cinacalcet (88), etelcalcetide (112), evocalcet (113), tecalcet (87), upacicalcet (118)
-cerfont	**corticotropin-releasing factor (CRF) receptor antagonists** crinecerfont (120), emicerfont (102), pexacerfont (97), tildacerfont (119), verucerfont (102)
-cianine	**indocyanine fluorescence dye group** nerindocianine (121), nizaracianine (125), omocianine (93), pafolacianine (124), pegsitacianine (125), pegulicianine (123) under (c) category: pudexacianinium chloride (122)

-(clo)sporin	**ciclosporin derivatives** ciclosporin (46), geclosporin (70), oxeclosporin (70), ruclosporin (114), voclosporin (97)
-copan	**complement receptor antagonists/ complement inhibitors** avacopan (114), danicopan (119), iptacopan (122), nomacopan (119), pelecopan (127), vemircopan (124) to be listed under (c) category: pegcetacoplan (120), zilucoplan (118)
-corat	**glucocorticoid receptor agonists** dagrocorat (111), fosdagrocorat (111), mapracorat (102), mizacorat (127), tomicorat (108), velsecorat (121)
-corilant	**glucocorticoid receptor antagonists (non-steroidal)** dazucorilant (125), exicorilant (119), miricorilant (119), nenocorilant (127), relacorilant (116), zavacorilant (125)
-delpar	**PPAR delta agonists** boxidelpar (126), delparantag (108), fonadelpar (114), mavodelpar (127), seladelpar (115)
-dil	*vasodilators*
-sudil	**Rho protein kinase inhibitors** belumosudil (123), cotosudil (123), fasudil (64), netarsudil (113), ripasudil (109), verosudil (112), zelasudil (128)
-espib	**heat shock protein (HSP) 90 inhibitors (other than –*mycin*)** cemdomespib (126), ganetespib (105), icapamespib (123), luminespib (108), onalespib (112), pimitespib (121), zelavespib (123)
-estrant	**estrogen antagonists, including estrogen receptor down-regulators** amcenestrant (122), bexirestrant (126), brilanestrant (115), camizestrant (125), elacestrant (115), fulvestrant (79), giredestrant (122), imlunestrant (126), palazestrant (128), rintodestrant (123), taragarestrant (127), vepdegestrant (127)
-fenicol	**antibacterial antibiotics, chloramphenicol analogues** azidamfenicol (14), cetofenicol (14), cloramfenicol pantotenate complex (14), florfenicol (54), racefenicol (20), sirpefenicol (126)
-fexor	**farnesoid X receptor agonists** cilofexor (119), nidufexor (118), omesdafexor (127), tropifexor (116), turofexorate isopropyl (103), vonafexor (122)

-fusp	**fusion proteins**[1] bintrafusp alfa (121), bizaxofusp (127), brenetafusp (128), cemavafusp (128), cinrebafusp alfa (121), clervonafusp alfa (120), dalutrafusp alfa (125), eciskafusp alfa (127), efdamrofusp alfa (125), ensomafusp alfa (125), gulgafafusp alfa (128), latikafusp (126), lepunafusp alfa (125), lorukafusp alfa (120), lunaxafusp (127), modakafusp alfa (122), nanrilkefusp alfa (126), nomlabofusp (126), onfekafusp alfa (118), oplunofusp (123), pabinafusp alfa (120), rozibafusp alfa (120), simlukafusp alfa (121), sotiburafusp alfa (128), tagraxofusp (118), tebentafusp (118), tividenofusp alfa (128), valanafusp alfa (118), vensobafusp alfa (128), vimekofusp (129)
-ganan	**antimicrobials, permeability increasing peptides** iseganan (85), lefleuganan (127), omiganan (89), peceleganan (126), pexiganan (78), upleganan (128), voxvoganan (126), zaloganan (129)
-golix	**gonadotropin releasing hormone (GnRH) antagonists** elagolix (99), linzagolix (118), merigolix (128), opigolix (118), relugolix (107), sufugolix (89)
-inurad	**urate transporter inhibitors** dotinurad (116), epaminurad (118), lesinurad (105), lingdolinurad (129), pozdeutinurad (129), puliginurad (127), ruzinurad (125), verinurad (111), xininurad (127)
-irine	**cytotoxic pyrrolobenzodiazepine dimers and analogues** camidanlumab tesirine (117), loncastuximab tesirine (117), mipasetamab uzoptirine (123), pivekimab sunirine (125), rolinsatamab talirine (119), rovalpituzumab tesirine (114), serclutamab talirine (120), tamrintamab pamozirine (120), vadastuximab talirine (113)
-ixafor-	**chemokine CXCR4 antagonists** balixafortide (112), burixafor (104), gallium (^{68}Ga) boclatixafortide (126), mavorixafor (118), motixafortide (120), plerixafor (93), yttrium (^{90}Y) anditixafortide (126)
-ixibat	**ileal bile acid transporter (IBAT) inhibitors, bile acid reabsorption inhibitors** barixibat (88), elobixibat (104), linerixibat (118), maralixibat chloride (113), odevixibat (119), ritivixibat (128), volixibat (113)
–leuton	**5-lipo-oxygenase inhibitors, anti-inflammatory** atreleuton (78), diroleuton (118), epeleuton (118), fenleuton (72), setileuton (101), zileuton (63)

[1] *A fusion protein is defined as a multifunctional protein derived from a single nucleotide sequence which may contain two or more genes or portions of genes with or without amino acid linker sequences. The genes should originally code for separate proteins, with at least two of them endowed with pharmacological action (e.g. action and targeting).* "Notes from the fusion protein Working Group", INN Working Document number 17.414 rev.

-madlin **E3 ubiquitin-protein ligase Mdm2 (Hdm2) inhibitors**
alrizomadlin (125), brigimadlin (128), navtemadlin (124), rebemadlin (125), siremadlin (119), sulanemadlin (123)
to be listed under category (c): idasanutlin (111), milademetan (117), serdemetan (101)

-meran **messenger RNA (mRNA)**
abdavomeran (124)*, acavameran (124), autogene cevumeran (122), enomimeran (123), fazulemeran (125), ganulameran (124)*, gindameran (123), nadorameran (113), ontasameran (123), pidacmeran (124)*, pomulmeran (123), vecilmeran (129)*, vibosameran (123), zapomeran (127)*, zeldesmeran (127)*, ziclumeran (127), zorecimeran (124)*
-tozinameran (124)*: ril*tozinameran* (126)*, fam*tozinameran* (128)*, rax*tozinameran* (129)*, pi*tozinameran* (129)*
-ufr*enmeran* (127)*, tegr*enmeran* (129)*
-*elasomeran* (125)*: im*elasomeran* (127)*, sec*elasomeran* (128)*, dav*esomeran* (128)*, andu*someran* (129)*, vint*esomeran* (129)*
**additional prop.INN Lists COVID-19 (special editions)*

-pixant **purinoreceptor (P2X) antagonists**
camlipixant (127), eliapixant (122), filapixant (122), gefapixant (118), sivopixant (123)

-prodil ***N*-methyl-D-aspartate (NMDA) receptor antagonists**
eliprodil (66), ifenprodil (27), onfasprodil (126), radiprodil (98), traxoprodil (86)
under (c) category: -nemdaz
nelonemdaz (121), rislenemdaz (116)

-(o)pterin **pteridine derivatives**
aminopterin sodium (04), fosdenopterin (121), ronopterin (113), sapropterin (63), sepiapterin (126)

-rasib **Ras protein inhibitors**
adagrasib (124), divarasib (127), fulzerasib (128), garsorasib (126), opnurasib (128), salirasib (97), sotorasib (123)

-rsen *antisense oligunucleotides*
-nersen **targeting neurological functions**
lexanersen (125), movronersen (125), nusinersen (112), rovanersen (125), rugonersen (125), tominersen (121), tadnersen (124), ulefnersen (127), zilganersen (126), zorevunersen (125)
under (b) category**:** cenersen (97)
under (c) category**:** baliforsen (116), casimersen (115), dematirsen (116), drisapersen (106), eteplirsen (103), golodirsen (115), inotersen (115), plenotersen (123), renadirsen (120), rimigorsen (116), sepofarsen (121), suvodirsen (121), varodarsen (116)

-sidenib **isocitrate dehydrogenase inhibitors**
enasidenib (113), ivosidenib (114), olutasidenib (120), safusidenib (126), vorasidenib (117)

stat enzyme inhibitors

-demstat **lysine-specific histone demethylase inhibitors**
bomedemstat (122), iadademstat (119), pulrodemstat (124), seclidemstat (118), vafidemstat (119), zavondemstat (128)

-becestat **beta secretase inhibitors**
atabecestat (117), elenbecestat (117), umibecestat (119), lanabecestat (116), verubecestat (112)

-folastat **inhibitors of folate hydrolase 1 (prostate-specific membrane antigen, PSMA)**
abefolastat tesaroxetan (129), flotufolastat (^{18}F) (123), iofolastat (^{123}I) (105), piflufolastat (^{18}F) (126), technetium (^{99m}Tc) trofolastat chloride (109), vidoflufolastat (^{18}F) (127)

-glustat **ceramide glucosyltransferase inhibitors**
duvoglustat (102), eliglustat (103), miglustat (85), nizubaglustat (128), sinbaglustat (121), venglustat (114)

-metostat **histone *N*-methyltransferase inhibitors**
igermetostat (129), lirametostat (123), onametostat (123), pemrametostat (123), pinometostat (112), tazemetostat (112), tulmimetostat (126), valemetostat (118)

-stinel ***N*-methly-D-aspartate (NMDA) receptor co-agonists**
apimostinel (115), gavestinel (77), licostinel (77), nevadistinel (129), rapastinel (111), risevistinel (129), zelquistinel (121)

-tide *peptides*

-dutide **oxyntomodulin analogues and other dual agonists of glucagon-like peptide receptor 1 (GLP-1R) and glucagon receptor (GCGR*)***
bamadutide (119), cotadutide (119),efinopegdutide (119), mazdutide (126), pegapamodutide (116), pemvidutide (126)

-enatide **glucagon-like peptide-1 receptor (GLP1R) agonists, exenatide (exendin-4) and analogues**
albenatide (114), efpeglenatide (111), exenatide (89), langlenatide (111), lixisenatide (99), pegsebrenatide (127), pegloxenatide (125), visepegenatide (129), vurolenatide (126*)*

-netide **neurological**
alirinetide (117), cibinetide (114), davunetide (100), nerinetide (119), obinepitide (96), orenetide (125), trofinetide (112)
under (b) category: diamfenetide (28)
under (c) category: doreptide (59), nemifitide (87), pareptide (38), vanutide cridificar (100)

-paratide **parathyroid hormone analogues**
abaloparatide (109), eneboparatide (127), palopegteriparatide (126), semparatide (80), teriparatide (50)

-pultide **peptides and proteins, used in pulmonary surfactants**
elopultide (121), lusupultide (80), redipultide (119), sinapultide (78), zelpultide alfa (126)

-tinib tyrosine kinase inhibitors

-ertinib **epidermal growth factor receptor (EGFR) inhibitors**
abivertinib (119), befotertinib (123), canertinib (87), epertinib (115), firmonertinib (129), lazertinib (117), mavelertinib (118), mifanertinib (128), mobocertinib (121), olafertinib (121), osimertinib (113), rezivertinib (122), sacibertinib (127), sunvozertinib (125), tuxobertinib (125), xiliertinib (121), zipalertinib (126), zongertinib (128), zorifertinib (121)

Under (b) category: ulixertinib (113), ravoxertinib (115) (Erk inhibitors)
Under (c) category: afatinib (104), olmutinib (114), erlotinib (85), gefitinib (85), mubritinib (90), nazartinib (114), mubritinib (90), nazartinib (114)

-trectinib **tropomyosin receptor kinase (TRK) inhibitors**
anizatrectinib (127), boditrectinib (128), emzeltrectinib (128), entrectinib (113), larotrectinib (115), paltimatrectinib (126), repotrectinib (120), selitrectinib (120), taletrectinib (123), utatrectinib (126)

-tirom(-) **antihyperlidaemics, thyromimetic derivatives**
acetiromate (30), axitirome (82), bentiromide (41), eprotirome (99), omzotirome (125), resmetirom (119), sobetirome (126)

-toclax **B-cell lymphoma 2 (Bcl-2) inhibitors**
imlatoclax (115), lacutoclax (129), lisaftoclax (125), mirzotamab clezutoclax (121), murizatoclax (122), navitoclax (103), obatoclax (94), pelcitoclax (122), sonrotoclax (128), tapotoclax (121), venetoclax (111)

-trep **transient receptor potential antagonists**
asivatrep (117), elismetrep (118), evifacotrep (125), libvatrep (124), mavatrep (111), motugivatrep (126)

-trombopag **thrombopoietin agonists**
avatrombopag (107),eltrombopag (94), lusutrombopag (104), rafutrombopag (127), totrombopag (97)

-turev **under the advanced therapy scheme for: oncolytic viruses**
canerpaturev (117), gebasaxturev (126), lerapolturev (125), suratadenoturev (123), tasadenoturev (117), teserpaturev (119)
under (c) category: enadenotucirev (111)

-vir		*antivirals*
	-capavir	**viral capsid and nucleocapsid inhibitors** bersacapavir (122), canocapavir (127), claficapavir (126), pocapavir (107), lenacapavir (121) under (c) category*:* pirodavir (63), vapendavir (106)
-vivint		**Wnt signaling inhibitors** cirtuvivint (123), foscenvivint (124), ipivivint (123), lorecivivint (119), tegavivint (118), teplinovivint (123)

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Amendments were also made in the following stems' definitions:

-eridine
from *analgesics, pethidine derivatives*
to *analgesics, pethidine derivatives and other synthetic small molecule μ-opioid receptor agonists*

kef
from *enkephalin agonists*
to *enkephalin, endorphin and dynorphin opioid δ, μ and κ receptor agonists*

-ilide
from *class III antiarrhythmics, sematilide derivatives*
to *class III antiarrhythmics, ~~sematilide derivatives~~*

-imus
from *immunosuppressants*, *other than antineoplastics*
to *immunosuppressants, ~~other than antineoplastics~~*

-isant
from *histamine H_3 receptor antagonists*
to *histamine H_3 receptor antagonists, inverse agonists*

-kinra
from *interleukin receptor antagonists*
to *interleukin receptor antagonists and interleukin antagonists*

-(o)nidine
from *antihypertensives, clonidine derivatives*
to *α_2 adrenoreceptor agonists*

-pressin
from *vasoconstrictors, vasopressin derivatives*
to *~~vasoconstrictors,~~ vasopressin analogues*

-pride
from *sulpiride derivatives*
to *sulpiride derivatives and analogues*

-prim
from *antimicrobials, dihydrofolate reductase (DHFR) inhibitors, trimethoprim derivatives*
to *antimicrobials, dihydrofolate reductase (DHFR) inhibitors, trimethoprim analogues*

-racetam (NEW)
from *amide* ***type*** *nootrope agents, piracetam derivatives*
to *amide ~~type~~ nootrope agents, piracetam type*

-renone
from *aldosterone receptor antagonists, spironolactone derivatives*
to *mineralocorticoid receptor (MR, MCR, aldosterone receptor) antagonists*

-siran
from *small interfering RNA*
to *small interfering RNA including siRNA, miRNA and piRNA*

under *-tant*
-netant
from *neurokinin NK3 receptor antagonists*
to *neurokinin NK3 and dual NK3-NK1 receptor antagonists*

under *-tide*
-glutide
from *glucagon-like peptide (GLP) analogues*
to *glucagon-like peptide (GLP) analogues and agonists*

-toclax (NEW) see above
from *B-cell lymphoma 2 (Bcl-2) inhibitors, antineoplastics*
to *B-cell lymphoma 2 (Bcl-2) inhibitors~~, antineoplastics~~*

Amendments were also made in the stem's infix:
-gromab (under -mab)
from *-grosmab*
for the designation of INN for monoclonal antibodies targeting skeletal muscle mass related growth factors and receptors

***-ki-* (under *-mab*)**
for the designation of INN for monoclonal antibodies targeting interleukins,
to cytokine and cytokine receptors

Please note that a new naming scheme for monoclonal antibodies has been adopted at the 73rd INN Consultation. The document can be retrieved here after and from our webpages at: https://cdn.who.int/media/docs/default-source/international-nonproprietary-names-(inn)/new_mab_-nomenclature-_2021.pdf?sfvrsn=207e78cb_12&download=true

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New INN monoclonal antibody (mAb) nomenclature scheme

Geneva, November 2021

International Nonproprietary Names (INN) Programme and Classification of Medical Product)

INN and Classification of Medical Products Unit
Health Product Policy and Standards Department (HPS)
Access to Medicines and Health Products Division (MHP)
World Health Organization, Geneva

Suffixes/stems

As the previous INN nomenclature scheme for monoclonal antibodies (mAb), this new INN mAb nomenclature scheme is used for all substances that contain an immunoglobulin variable domain that binds to a defined target, and that is composed of only immunoglobulin-derived pharmacologically active components. The suffix is preceded by an infix that indicates the target class.

However, in contrast to the previous INN mAb nomenclature scheme, the new INN mAb nomenclature scheme divides the substances that contain an immunoglobulin variable domain into four groups, there being three groups for monospecific immunoglobulins and one for bi- and multi-specific immunoglobulins, independent of their type, shape and form.

Group 1 **-*tug* for *unmodified immunoglobulins***   Monospecific full length and Fc unmodified[1] immunoglobulins of any class. Molecules which might occur as such in the immune system. Including: - IgG, IgA, IgM, IgD, IgE   - only allelic variants   - Glycoengineering without mutation   - C-terminal lysine deletion without any other mutation in the Fc region
Group 2 **-*bart* for *antibody artificial***   Monospecific full length immunoglobulins with engineered constant domains (CH1/2/3).   Monospecific full length immunoglobulins that contain any point mutation introduced by engineering for any reason anywhere (hinge, new glycan attachment site, mixed allelic variants which would not occur in nature, altered complement binding, altered FcRn binding, altered Fc-gamma receptor binding, etc.)   *e.g*. IGHG4 with S>P mutation, stabilized IgA
Group 3 **-*mig* for *multi-immunoglobulin***   Bi- and multi-specific immunoglobulins regardless of the format, type or shape (full length, full length plus, fragments)
Group 4 **-*ment* for *fragment***   All monospecific domains, fragments of any kind, derived from an immunoglobulin variable domain (all monospecific constructs that do not contain an Fc domain)

[1] Do not contain any amino acid differences with the native sequence (constant region amino acid changes by comparison with the closest genomic C gene and allele).

Note1: Immunoglobulin fusions are only included in the monoclonal antibody nomenclature scheme if both domains have immunoglobulin derived variable domains (*eg*. mAb fused with a cytokine is under the *-fusp* nomenclature scheme).

Note2: Antibody-drug conjugates (ADC) also follow this new mAb nomenclature scheme and no special suffix is added, as the second word indicates that the substance is a conjugate.

Infixes

The mechanisms of monoclonal antibodies are complex, may be different for different indications may and might not be completely understood during development. Therefore, the infix is assigned according to the proposed known mode of action at the time of the INN request.

The changes for the new scheme are in green.

Infix	Definition
-ami-	serum amyloid protein (SAP)/amyloidosis *(pre-substem)*
-ba-	bacterial
-ci-	cardiovascular
-de-	metabolic or endocrine pathways
-eni-	enzyme inhibition
-fung-	fungal
-gro-	skeletal muscle mass related growth factors and receptors *(pre-substem)*[1]
-ki-	cytokine and cytokine receptor[2]
-ler-	allergen
-sto-	immunostimulatory
-pru-	immunosuppressive
-ne-	neural
-os-	bone
-ta-	tumour
-toxa-	toxin
-vet-	veterinary use *(sub-stem)*
-vi-	viral

[1] At the 69th INN Consultation, the infix changed from *-gros-* to *-gro-* to avoid a conflict with the infix *-os-*.

[2] At the 70th INN Consultation, it was decided that the antibodies targeting an interleukin receptor would also have the *-ki-* infix. The names discussed at this Consultation are included in INN Proposed List 124.