

World Health Organization  
**Raffaella Balocco**  
INN Programme Manager  
Quality Assurance & Safety :  
Medecines  
CH 1211 GENEVA 27  
SUISSE

Paris, November 15, 2018

## Prescrire's contribution to the WHO consultation on List 119 of proposed INNs

*Prescrire* is an independent continuing education organisation for healthcare professionals. It is wholly funded by its subscribers, carries no advertising, and receives no other financial support whatsoever.

Both independently since 1981, and with others as part of the Medicines in Europe Forum, the International Society of Drug Bulletins (ISDB) and the International Medication Safety Network (IMSN), *Prescrire* has been advocating the systematic use by healthcare professionals and patients of international nonproprietary names (INNs), which are clearer, safer and more informative than drug brand names (1-6).

**Making INNs safer.** The principles underlying the creation of INNs are the same that apply to the prevention of medication errors: standardisation, differentiation, and facilitation of logic and redundancy checks (7).

However, even with the INN system there is a residual risk of confusion, partly owing to the sheer number of INNs now in circulation. A report from the Council of Europe, which recommends the use of INNs, calls for active participation in the public consultations on proposed INNs organised by the World Health Organization (WHO), in order to identify any risk of confusion during their clinical use (8). Our review group, consisting of members of *Prescrire's* editorial staff, including hospital- and community-based health professionals, joined by lecturers in pharmacy and medicine from Marseille University Hospital and Marseille School of Pharmacy, has examined List 119 in order to participate in the public consultation on this latest list of proposed INNs, published in July 2018 (a)(9).

**Our critical analysis of the proposed INNs.** Our analysis of the 120 INNs proposed in List 119, and 4 amendments to INNs proposed in previous lists, was based on the following resources: the 2013 list of common stems and its addenda; the INN database and the WHO's lists of pre-stems, biological and biotechnological substances, and radicals; the list of planned stems proposed by the United States Adopted Names (USAN) Council; a database of drugs marketed in France, which enables searches on both brand names and INNs; a reference database of drugs used throughout the world; and *Prescrire's* in-house monitoring of the literature (10-18).

The first step of *Prescrire's* collective review was to identify INNs or brand names of marketed drugs that could potentially be confused with the INNs proposed in List 119. In each case, the participants then assessed the likelihood and clinical consequences of a medication error or misunderstanding arising through this mechanism, listing their arguments. When clinical consequences were foreseeable, the participants were also invited to suggest solutions to reduce the risk of confusion.

**Prescrire**  
83 boulevard Voltaire  
75558 PARIS CEDEX 11  
FRANCE

Tél. : (33) (0)1 49 23 72 80  
Fax : (33) (0)1 47 00 33 20  
contact@prescrire.org

Site internet  
Web site  
www.prescrire.org

Relations Abonnés :  
Abonnements  
Subscription Department  
Tél. : (33) (0)1 49 23 72 86  
Fax : (33) (0)1 49 23 76 48  
relationsabonnes@prescrire.org  
international@prescrire.org

Formations Prescrire  
Tél. : (33) (0)1 49 23 72 90  
Fax : (33) (0)1 49 23 76 48  
formations@prescrire.org

Association Mieux Prescrire

Organisme indépendant  
de formation permanente  
des soignants

Independent organisation  
continuing education  
for health professionals

Association loi de 1901  
n° 86/4331 - JO 21/01/1987  
(Statuts sur demande)  
Org DPC n° 1358  
Org FC 11 751 711 075  
N° TVA : FR 48 340647619  
SIRET 340 647 619 00014  
Code NAF : 9499Z  
RIB La Banque Postale Paris  
BIC : PSST FRPPPAR  
IBAN :  
FR44 2004 1000 0100 6120 5H02 022

**Another long list.** With 120 proposed INNs and 4 amendments, List 119 is one of the longest *Prescrire* has examined.

Our examination of List 119 provided an opportunity to identify some pre-stems: **-becestat** for  $\beta$  secretase inhibitors; **-caftor** for cystic fibrosis transmembrane regulator (CFTR) protein modulators; **-cerfont** for corticotropin-releasing factor type-1 (CRF1) receptor antagonists; **-ertinib** for epidermal growth factor receptor (EGFR) inhibitors; **-ixibat** for ileal bile acid transporter (IBAT) inhibitors, bile acid reabsorption inhibitors; **-pirdine** for serotonin receptor antagonists; and **-tirom(-)** for antihyperlipidaemic thymomimetic derivatives.

This list also includes some planned stems proposed by the US drug nomenclature committee, the USAN Council: **-alap** for aldehyde traps; **-copan** for complement receptor inhibitors; **-corilant** for glucocorticoid receptor antagonists (not glucocorticoids); **-dostat** for indoleamine 2,3-dioxygenase inhibitors; **-dutide** for oxyntomodulin analogues; **-forant** for histamine H<sub>4</sub> receptor antagonists; **-netide** for peptides and glycopeptides for which neurological uses have been planned; **-nod** for nitrogen oxide donors; **-padon** for dopamine D1 receptor agonists/partial agonists; **-pultide** for peptides used as pulmonary surfactants; **-semtiv** for skeletal muscle troponin activators; **-tristat** for tryptophan hydroxylase inhibitors; and **-vivint** for WNT pathway inhibitors.

### Formal objections

None of the risks of confusion or misunderstanding associated with the INNs proposed in List 119 were of sufficient concern to warrant a formal objection.

**The abiding risk associated with the naming of monoclonal antibodies conjugated to active substances.** We remain very concerned about the risks associated with the two-term INNs given to monoclonal antibodies conjugated to cytotoxic drugs. If healthcare professionals do not know the precise meaning of the second term, which they may assume refers to a radical devoid of pharmacological activity rather than a second active substance, dosing errors can occur through administration of the wrong product. The proposed INNs *rolinsatamab talirine* and *tabituximab barzuxetan* add to the list of similarly constructed INNs for antibody–drug conjugates against which *Prescrire* has filed objections in previous consultations (19).

We formally acknowledge that, while recognising the problem, the WHO INN Programme does not want to revise the nomenclature of these conjugated compounds, on the grounds that the rules were established a long time ago (20). This amounts to shifting the task of risk mitigation onto pharmaceutical companies, regulatory agencies, healthcare establishments and organisations, and health professionals, requiring them to devise measures to reduce the number of patients harmed through confusion between these INNs, such as: aiding discrimination between these products through different packaging or labelling, and aiding discrimination between their INNs, for example by appending the brand name. This leads to the paradoxical situation in which it is safer to use brand names than INNs.

**Why not take the revision of the monoclonal antibody nomenclature scheme further?** The new nomenclature scheme for monoclonal antibodies, which includes discontinuation of the species substem, is a welcome development (21). However, some of the participants in our review group would like to see the “target class” substems of this new nomenclature developed further, to make the INNs of monoclonal antibodies more informative. For example, health professionals can tell from the substem **-ci-** in the proposed INNs *abelacimab*, *dilpacimab*, *frovocimab*, *olinvacimab* and *osocimab* that these drugs target the cardiovascular system, but not that they also have immunomodulatory, antineoplastic, blood coagulation factor inhibiting, anticoagulant or lipid-lowering properties.

Similarly, some participants were concerned by the apparent lack of specificity of the target substems **-li-** and **-ta-** in the proposed INNs *budigalimab*, *cemiplimab*, *dostarlimab*, *tabituximab* [containing the **-t(u)-** target substem of the old nomenclature] and *toripalimab*, each described as an “immunomodulator, antineoplastic”. Are they immunomodulators and/or antineoplastics? And in which therapeutic areas will they be used?

Prescrire  
83 boulevard Voltaire  
75558 PARIS CEDEX 11  
FRANCE  
Tél. : (33) (0)1 49 23 72 80  
Fax : (33) (0)1 47 00 33 20  
contact@prescrire.org

Site internet  
Web site  
www.prescrire.org

Relations Abonnés :  
Abonnements  
Subscription Department  
Tél. : (33) (0)1 49 23 72 86  
Fax : (33) (0)1 49 23 76 48  
relationsabonnes@prescrire.org  
international@prescrire.org

Formations Prescrire  
Tél. : (33) (0)1 49 23 72 90  
Fax : (33) (0)1 49 23 76 48  
formations@prescrire.org

Association Mieux Prescrire

Organisme indépendant  
de formation permanente  
des soignants

Indépendant organisation  
continuing education  
for health professionals

Association loi de 1901  
n° 86/4331 - JO 21/01/1987  
(Statuts sur demande)  
Org DPC n° 1358  
Org FC 11 751 711 075  
N° TVA : FR 48 340647619  
SIRET 340 647 619 00014  
Code NAF : 9499Z  
RIB La Banque Postale Paris  
BIC : PSST FRPPPAR  
IBAN :  
FR44 2004 1000 0100 6120 5H02 022

## Comments

Our review group identified a number of proposed INNs that could generate medication errors for a variety of reasons: confusion with a brand name; confusion with another INN; confusion between their suffix and an existing stem; or confusion due to the absence of an expected stem.

**Confusion with a brand name.** Some INNs proposed in List 119 could be confused with a brand name, in particular: *abelacimab*, *resmetirom*, *rovafovir etalafenamide* and *tirzepatide*.

When selecting drugs from an alphabetical menu, the proposed INN *abelacimab* could be confused with Abelcet<sup>o</sup>, a brand name used for *amphotericin B* in many countries.

The proposed INN *resmetirom* could be confused with the brand name Esmeron<sup>o</sup> of the neuromuscular blocker *rocuronium*, marketed under this name in at least 38 countries. Without knowing the route of administration of *resmetirom*, it is difficult to assess the likelihood of confusion between these drugs. However, unintentional administration of a neuromuscular blocker would have catastrophic consequences for the patient.

The proposed INN *rovafovir etalafenamide* shares the first four letters of the brand name Rovalcyte<sup>o</sup> (*valganciclovir*). Despite the marked difference between the two INNs, the likelihood of confusing these drugs is increased by the fact that both have antiviral properties.

Resemblance was also noted between the proposed INN *tirzepatide* and the brand name Zepatier<sup>o</sup> (*elbasvir+grazoprevir*).

**Confusion with another INN.** Some of the INNs proposed in List 119 are liable to confusion with other INNs, in particular: *abelacimab*, *asalhydromorphone*, *aticaprant*, *azelaprag*, *fosgemcitabine palabenamide*, *fosifloxuridine nafalbenamide*, *frovocimab*, *masupirdine*, *mivavotinib*, *nomacopan*, *reproxalap*, *setogepram* and *tirzepatide*.

The proposed INN *abelacimab* could be confused with the INN *abciximab*, as they have the same prefix and almost identical suffixes.

The proposed INN *asalhydromorphone* could be confused with the INN *hydromorphone*, with a risk of dosing errors, although the severity of the consequences is difficult to assess without knowing their relative potency. It is important that the INN Programme ensures drug regulatory agencies are aware of this risk, and that the strengths of all marketed products are expressed in the same way, as *hydromorphone* base for example.

A risk of confusion through visual and phonetic similarity was noted between the proposed INN *aticaprant* and the INNs *apixaban* and *icatibant*.

In an alphabetical menu, the proposed INN *azelaprag* would appear immediately above the INN *azelastine* and might therefore be selected in error in its place.

The proposed INN *fosgemcitabine palabenamide* could be confused with the INN *gemcitabine*, i.e. the drug from which it is derived. The severity of the consequences of such an error would depend on their relative potency. Similarly, a risk of confusion was noted between the proposed INN *fosifloxuridine nafalbenamide* and the INN *floxuridine*, although the latter no longer appears to be marketed. When a drug is modified by a radical to form a salt or ester prodrug, it is crucial that health professionals understand how the radical modulates the dose received by altering its pharmacokinetics or pharmacodynamics.

A small risk of confusion was noted between the proposed INN *frovocimab* and the INN *frovatriptan*, which have almost identical and therefore insufficiently distinctive prefixes.

A risk of confusion was identified between the proposed INN *masupirdine* and the INNs *mesudipine* and *manidipine*, due to orthographic and phonetic similarities. The risk is compounded by the potential for confusion between the pre-stem **-pirdine**, used for serotonin receptor antagonists, and the stem **-dipine**, used for calcium channel blockers, which we reported in our responses to Lists 102 and 116 (19).

The similarity of the prefix of the proposed INN *mivavotinib* to that of the INN of the neuromuscular blocker *mivacurium* and its brand name Mivacron<sup>o</sup> caused concern. However, the probable route of administration of *mivavotinib* markedly reduces the likelihood of confusion errors. The consequences of errors involving neuromuscular blocking drugs are potentially catastrophic (risk of death through respiratory paralysis). In the interests of patient safety, INNs should never be liable to confusion with the INN or brand name of a neuromuscular blocker.

Prescrire  
83 boulevard Voltaire  
75558 PARIS CEDEX 11  
FRANCE

Tél. : (33) (0)1 49 23 72 80  
Fax : (33) (0)1 47 00 33 20  
contact@prescrire.org

Site internet  
Web site  
www.prescrire.org

### Relations Abonnés :

Abonnements  
Subscription Department  
Tél. : (33) (0)1 49 23 72 86  
Fax : (33) (0)1 49 23 76 48  
relationsabonnes@prescrire.org  
international@prescrire.org

Formations Prescrire  
Tél. : (33) (0)1 49 23 72 90  
Fax : (33) (0)1 49 23 76 48  
formations@prescrire.org

Association Mieux Prescrire

Organisme indépendant  
de formation permanente  
des soignants

Independent organisation  
continuing education  
for health professionals

Association loi de 1901  
n° 86/4331 - JO 21/01/1987  
(Statuts sur demande)  
Org DPC n° 1358  
Org FC 11 751 711 075  
N° TVA : FR 48 340647619  
SIRET 340 647 619 00014  
Code NAF : 9499Z  
RIB La Banque Postale Paris  
BIC : PSST FRPPAR  
IBAN :  
FR44 2004 1000 0100 6120 5H02 022

The proposed INN *nomacopan*, for a complement factor C5 inhibitor, could be confused with the INNs *nonacog alfa*, *nonacog beta pegol* and *nonacog gamma*. Five of the seven letters in the first term are shared with *nomacopan*, while the marked typographic resemblance between the two letters that differ (“n” versus “m”, and “g” versus “p”) enhances their visual similarity. The fact that blood products are usually stored together increases the likelihood of a confusion error.

The proposed INN *reproxalap* could be confused with the INN *eprosartan*, due to the similarity of their prefixes, apart from the initial letter “r”, and because *reproxa-* and *epros-* sound extremely similar in French.

Many of the participants in our review group reported a risk of confusion between the proposed INN *setogepgram* and the INNs *citalopram* and *escitalopram*. It could also be confused with *Sérogram*<sup>o</sup>, a brand name for *citalopram*. Furthermore, although *setogepgram* is claimed to have anti-inflammatory and antifibrotic properties, it lacks a corresponding stem, and the participants in our review group assumed it to be a so-called “selective” serotonin reuptake inhibitor.

The proposed INN *tirzepatide* resembles the INN *tinzaparin*, a risk that will be compounded if their route of administration is similar.

**Confusion between a suffix and a stem.** Two INNs proposed in List 119 that lack a stem have suffixes, *-oxazine* and *-gepram*, that could be confused with existing stems.

The suffix *-oxazine* in the INN *brilaroxazine* could be confused with the stem **-oxacin** (**-oxacine** in French), used for antibiotics derived from nalidixic acid, also known as quinolones.

The suffix *-gepram* in the proposed INN *setogepgram* could be confused with the new stem **-gepant**, used for calcitonin gene-related peptide (CGRP) receptor antagonists.

**Confusion due to absence of an expected stem.** The INNs *bamadutide*, *cotadutide* and *tirzepatide* have been proposed for antidiabetic drugs. The participants in our review group were surprised by the absence of the stem **-gli-**, which is generally present in the INNs of drugs for which this property is claimed. They felt that the absence of the expected stem in these proposed INNs compromises the ability of users to understand their pharmacological effect.

**Amendments.** Amendments to INNs proposed in previous lists are subjected to the same risk analysis as newly proposed INNs. Concerns were raised about two of the four amendments in List 119: *lorecevivint* and *oxycodogol*.

The INN *lorecevivint* replaces *adavivint*, proposed in List 117. In our response to that list, we commented on the risk of wrong-drug errors when selecting drugs from an alphabetical menu due to its similarity and proximity to with *Adavin*<sup>o</sup> (19). However, the new name is liable to confusion with the brand name *Recivit*<sup>o</sup> (*fentanyl*), especially when written.

The INN *oxycodogol* replaces *loxicodogol* (List 117). By dropping the initial “l” and replacing the “i” with a “y”, the amended name is liable to confusion with the INN *oxycodone* (the first 6 letters are identical) as well as its brand name *Oxycontin*<sup>o</sup>. Their proximity in an alphabetical menu creates a high risk of selection errors, compounded by the fact that they are both opioid receptor agonists. The consequences of confusing them are difficult to assess, but if their potencies differ, as is likely, a risk of overdose will exist.

**In summary.** Our examination of List 119 of proposed INNs confirms the major role of education in helping health professionals decipher and understand INNs.

This list gave rise to fewer comments than previous lists to point out proposed INNs identified as liable to confusion or difficult to decipher. However, problems identified by health professionals must continue to be taken into account, including: the increasing complexity of INNs, an issue raised by many of our reviewers; the fact that some therapeutic classes have reached saturation point; the role of radicals in altering drugs’ pharmacokinetic or pharmacodynamic properties; and the advantages of INNs that provide more information about the drug’s indications and properties, while remaining simple and easy to memorise.

Despite the fact that our group considered no formal objections were necessary, the nomenclature for monoclonal antibodies conjugated to pharmacologically active drugs is an issue that remains unresolved and continues to concern us.

Prescrire  
83 boulevard Voltaire  
75558 PARIS CEDEX 11  
FRANCE

Tél. : (33) (0)1 49 23 72 80  
Fax : (33) (0)1 47 00 33 20  
contact@prescrire.org

Site internet  
Web site  
www.prescrire.org

Relations Abonnés :  
Abonnements  
Subscription Department  
Tél. : (33) (0)1 49 23 72 86  
Fax : (33) (0)1 49 23 76 48  
relationsabonnes@prescrire.org  
international@prescrire.org

Formations Prescrire  
Tél. : (33) (0)1 49 23 72 90  
Fax : (33) (0)1 49 23 76 48  
formations@prescrire.org

Association Mieux Prescrire

Organisme indépendant  
de formation permanente  
des soignants

Independant organisation  
continuing education  
for health professionals

Association loi de 1901  
n° 86/4331 - JO 21/01/1987  
(Statuts sur demande)  
Org DPC n° 1358  
Org FC 11 751 711 075  
N° TVA : FR 48 340647619  
SIRET 340 647 619 00014  
Code NAF : 9499Z  
RIB La Banque Postale Paris  
BIC : PSST FRPPPAR  
IBAN :  
FR44 2004 1000 0100 6120 5H02 022

Healthcare professionals and patients can only think and act successfully in terms of INNs when these names are devised and taught in a rigorous, coherent and effective way, and when they are intelligible. The School of INN will undoubtedly occupy an important educational role in this teaching.



Bruno Toussaint  
Publishing Director

**Review produced collectively by the Prescrire Editorial Staff:  
no conflicts of interest  
©Prescrire**

*a- This response was prepared using the resources of the entire Prescrire team. Head of team analysis and preparation: Éric Bel (pharmacist). Members of the Prescrire editorial team who made a particular contribution to this review: Anne Americh (pharmacist); Élodie Artielle-Beaucamp (pharmacist); Julie Bontemps (pharmacist); Helen Genevier (translator); Christine Guilbaud (pharmacist); Marie-France Gonzalvez (pharmacist); Mélanie Hardy (pharmacist); Sébastien Hardy (pharmacist); Fabienne Jourdan (doctor); Laurence Le Quang Trieu (pharmacist); Loumi Nadjat (professor, pharmacologist); Florent Macé (pharmacist); Ève Parry (pharmacist); and Étienne Schmitt (pharmacist). Contributors from Marseille University Hospital Pharmacy and Marseille School of Pharmacy: Pascal Rathelot (professor, hospital consultant); Christophe Curti, Manon Roche (senior lecturers, hospital consultants); Fanny Matthias (teaching and research assistant); and Melissa Abbes, Théau Durepaire, Tiffany Kabac, Vincent Walter (pharmacy residents).*

Prescrire  
83 boulevard Voltaire  
75558 PARIS CEDEX 11  
FRANCE

Tél. : (33) (0)1 49 23 72 80  
Fax : (33) (0)1 47 00 33 20  
contact@prescrire.org

Site internet  
Web site  
www.prescrire.org

#### Relations Abonnés :

Abonnements  
Subscription Department  
Tél. : (33) (0)1 49 23 72 86  
Fax : (33) (0)1 49 23 76 48  
relationsabonnes@prescrire.org  
international@prescrire.org

Formations Prescrire  
Tél. : (33) (0)1 49 23 72 90  
Fax : (33) (0)1 49 23 76 48  
formations@prescrire.org

#### Association Mieux Prescrire

Organisme indépendant  
de formation permanente  
des soignants

Independant organisation  
continuing education  
for health professionals

## References

- 1- Prescrire Editorial Staff "Think INN, prescribe INN, dispense INN: good professional practice" *Prescrire Int* 2000; **9** (50): 184-190.
- 2- Prescrire Editorial Staff "Informed decisions: think of the INN" *Prescrire Int* 2005; **14** (78): 122.
- 3- Prescrire Rédaction "Patients-soignants: priorité à la DCI" <http://www.prescrire.org/cahiers/dossierDciAccueil.php>
- 4- International Society of Drug Bulletins (ISDB) "Special issue on INNs" *ISDB Newsletter* November 2006; **20** (3): 27 pages.
- 5- International Medication Safety Network (IMSN) "Improving the safety of international non-proprietary names of medicines (INNs)" November 2011; 5 pages.
- 6- Prescrire Rédaction "Ordonnance: la dénomination commune internationale (DCI) au quotidien" *Rev Prescrire* 2012; **32** (346): 586-591.
- 7- Prescrire Editorial Staff "Drug regulatory agencies maintain confusion between brand names" *Prescrire Int*. 2008; **17** (94): 83-86.
- 8- Council of Europe - Expert Group on Safe Medication Practices "Creation of a better medication safety culture in Europe: building up safe medication practices" Initial version of the report published online 19 March 2007: 257 pages.
- 9- WHO "Proposed international nonproprietary names: List 119" *WHO Drug Information* 2018; **32** (2): 283-398.
- 10- WHO "The use of stems in the selection of International Nonproprietary Names (INN) for pharmaceutical substances" WHO/EMP/RHT/TSN/2013.1 + Add. May 2018; 192+8 pages.
- 11- WHO "International nonproprietary names (INN) for pharmaceutical substances" mednet.who.int.
- 12- WHO "Pre-stems: Suffixes used in the selection of INNs – May 2018; 10 pages.
- 13- WHO "International Nonproprietary Names (INN) for biological and biotechnological substances" Update 2016.1; 80 pages.
- 14- WHO "International Nonproprietary Names (INN) for pharmaceutical substances. Names for radicals, groups & others - Comprehensive list" Update 2015.1; 80 pages.
- 15- United States Adopted Names Council "USAN Stem List" [www.ama-assn.org/resources/doc/usan/x-pub/stem-list-cumulative.xlsx](http://www.ama-assn.org/resources/doc/usan/x-pub/stem-list-cumulative.xlsx).
- 16- Thériaque database. <http://www.theriaque.org>
- 17- Martindale: The Complete Drug Reference. <https://about.medicinescomplete.com/publication/martindale-the-complete-drug-reference/>
- 18- ANSM: Répertoire des Spécialités Pharmaceutiques. <http://agence-prd.ansm.sante.fr/php/ecodex/>
- 19- Prescrire Editorial Staff "Prescrire's responses to the WHO's consultations on proposed INNs". <http://english.prescrire.org/en/79/549/49236/4221/ReportDetails.aspx>
- 20- Balocco Mattavelli R "Letter to Prescrire" 30 August 2016: 28 pages.
- 21- WHO "Working Group Meeting on Nomenclature for Monoclonal Antibodies (mAb)" Geneva, 6-7 October 2008; 5 pages.