Prescrire’s contribution to the WHO consultation on List 109 of proposed INNs

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As an active member of the Medicines in Europe Forum, the International Society of Drug Bulletins (ISDB) and the International Medication Safety Network (IMSN), Prescrire has long been advocating the routine use, by both healthcare professionals and patients, of international nonproprietary names (INNs), which are more informative, safer and clearer than brand names (1-5).

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 (6).

However, even with the INN system there is a residual risk of confusion between INNs, between INNs and brand names, and eventually misunderstanding. 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 (7). The editorial staff of Prescrire and members of the not-for-profit organisation Association Mieux Prescrire are participating in this phase of the consultation on List 109, which was published in July 2013, by examining these proposed INNs (8).

Our critical analysis of the proposed INNs. Our analysis of the 87 proposed INNs of List 109 was based on the 2011 list of common stems, on the INN database, on a database of drugs marketed in France, which enables searches on both brand names and INNs, and on Prescrire’s own data search (9-13).

Prescrire used a two-step Delphi method. First, the participants compiled a list of potentially contentious INNs, along with the reasons for their doubts. For each of the 30 proposed INNs selected for further scrutiny in this first step, the participants assessed the risk of confusion and/or misunderstanding, along with the potential clinical consequences of such errors. Finally they decided for each of these 30 contentious INNs whether a simple comment or a formal objection was more appropriate, and listed their arguments.
**More innovation.** While the previous list contained 74 proposed INNs, List 109 is longer and includes: 35 proposed INNs whose common stems have been presented in la revue *Prescrire* (40%); 15 proposed INNs whose common stems had not yet been presented at the start of our analysis of List 109 (17%); 35 novel proposed INNs or stems (40%); 2 variants, such as salts and isomers (2%); and no amendments to INNs proposed in previous lists. The graph plotted to monitor *Prescrire*’s contributions to the WHO’s public consultations on proposed INNs shows that, in comparison with previous consultations, List 109 included more novel proposed INNs or common stems.

The examination of a list of proposed INNs provides an opportunity to identify some pre-stems, of which List 109 includes: **-calcet/-calcet**- (in velcalcetide and also in cinacalcet, already authorised) for calcium-sensing receptor agonists; **-ciclib** (in palbociclib, riviciclib, roniciclib and voruciclib) for cyclin-dependent kinase inhibitors; **-fensine** (in liafensine, and also in nomifensine, withdrawn by the company in 1986 following cases of hemolytic anemia, some of them leading to death) for antidepressants (a norepinephrine, serotonin, dopamine reuptake inhibitor) (14); **-gepant** (in rimegepant and ubrogepant) for CGRP (calcitonin gene-related peptide) receptor antagonists; **-glurant** (in basimglurant, remeglurant and decoglurant) for metabotropic glutamate receptor antagonists; **-lisib** (in acalisib, panulisib and taselisib) for antineoplastic phosphatidylinositol 3-kinase inhibitors; **-metinib** (in binimetinib and ralimetinib) for antineoplastic MEK tyrosine kinase inhibitors; **-nesib** (in filanesib) for kinesin inhibitors; **-opran** (in axelopran) for µ-opioid receptor antagonists; **-piprant** (in asapiprant and fevipiprant, and also in laropiprant, withdrawn from the market) for non-prostanoid prostaglandin receptor antagonists; and **-rafenib** (in encorafenib, and also in regorafenib, sorafenib, vemurafenib, already authorised) for Raf kinase inhibitors (7,10).

Finally, the examination of List 109 of proposed INNs provided an opportunity to discover some pre-stems proposed by the US drug nomenclature committee (USANC: United States Adopted Names Council): **-asvir** for inhibitors of the hepatitis C virus protein NS5A, in ledipasvir and ombitasvir; **-folastat** for prostate-specific membrane antigen (PSMA) inhibitors, in technetium $^{99m}$Tc trofolastat chloride; **-pansel** for cell adhesion inhibitors that are P-selectin antagonists, in rivipansel; **-paratide** for parathyroid hormone analogues, in abaloparatide; and **-vatrep** for non-opioid analgesics that are vanilloid 1 receptor (TRPV1) antagonists, in mavatrep.
Comments

Some proposed INNs generate a risk of medication errors, for a variety of reasons: some could be confused with other INNs, particularly those that share similarity at the start of their names; some stems are easily confused with other stems; some INNs can be confused with brand names; and some common stems or INNs are difficult to interpret. Hence the following comments.

Confusion with other INNs. Some proposed INNs could be confused with existing INNs with which they share similarity at the start of the name, particularly: dasabuvir, filanesib and idarucizumab.

Dasabuvir could be confused with dasatinib, idarucizumab with idarubicin, and filanesib with finasteride. The latter two share additional phonetic similarity in French, since they contain the same vowel sounds in the same order. One way proposed to prevent confusion between these INNs would be to highlight the common stem, for example by using upper-case (“Tall Man”) lettering: dasaBUVIR, filaNESIB and idaruCIZUMAB (15).

Confusion between stems. Some of the proposed INNs could generate errors due to similarity between their common stem and another stem, particularly the proposed INNs containing the common stems -ciclib and -piprant.

The pre-stem -ciclib, adopted for cyclin-dependent kinase inhibitors and present in 4 INNs proposed in List 109 (palbociclib, riviciclib, roniciclib and voruciclib), was considered very similar to the stem -cycline, particularly when pronounced in French. Tetracycline derivatives form a large drug class and are in frequent use, but the risk of confusion, identified by all of our participants, must not be overlooked. On the other hand, the suffix “ib” is a useful aid to understanding several common stems, by indicating that they are inhibitors: -anib, -coxib, -imibe, -rafenib, -tib and -sertib; it is important that healthcare professionals are taught these helpful tips (16).

Similarly, the pre-stem -piprant, adopted for non-prostanoid prostaglandin receptor antagonists, in asapiprant and fevipiprant, could be confused with the common stem -pitant, which denotes neurokinin NK1 (substance P) receptor antagonists; this risk of error was already reported by Prescrire for setipiprant and vidupiprant during our analysis of List 104 of proposed INNs (17).

Confusion with brand names. Some of the proposed INNs resemble the brand names of drugs already marketed in France, in particular: abecomotide, doravirine, eldelumab, mavatrep, vedroprevir and velcal cetide. The risk of confusion between look-alike/sound-alike names is increased when similarity at the start of their names places them close to one another in situations where drugs are arranged alphabetically (on a computer screen or shelf), resulting in selection errors.

The close resemblance between velcal cetide and Velcade° (bortezomib) (5 letters in common) should have been identified already, when screening for similarity with trademarks. Our participants considered lodging a formal objection against velcalcetide on these grounds. If velcal cetide becomes a recommended INN, it will constitute another reason for encouraging the use of INNs, because velcalcetide could not be confused with bortezomib.

Doravirine is a similar case, since it contains the entire brand name Oravir° (famciclovir). Vedroprevir could be confused with Vedrop° (tocofersolan) if this antiviral is marketed in oral liquid form, particularly on paediatric wards where tocofersolan may be used concomitantly. Systematic use of INNs and stating the indication on the prescription might help prevent this type of error.

Similarity was also noted between eldelumab and Eldisine° (vindesine). Systematic use of INNs would prevent confusion between vindesine and eldelumab however; and in situations where INNs and brand names are used side by side, eldelumab would appear in
an alphabetical list before Eldisine®, thus reducing the risk of accidentally selecting a vinca alkaloid although it still exists a risk of inadvertent selection of a monoclonal antibody.

A risk of confusion was also identified between abecomotide and Bécotide® (beclometasone), an inhaled steroid, and between mavatrep and Moviprep®, a laxative combination used for bowel cleansing. The risk was considered low however, due to presumed differences in their dosage forms in the first case, and in their indications and routes of administration in the second.

**INNs that could be misinterpreted.** Several proposed INNs derived from existing INNs could be misunderstood, for example: damoctocog alfa pegol, eftrenonacog alfa, oreptacog alfa (activated), paclitaxel trevatide and ropeginterferon alfa-2b.

The most worrying risk is confusion between paclitaxel and paclitaxel trevatide, because it could lead to overdose or underdose, a similar risk already exists between trastuzumab and trastuzumab emtansine (18). In these cases, it is particularly important to ensure that INN users understand the added term, to highlight it on packaging and labelling, and to accentuate the differences between these complex INNs and the INNs from which they are derived in computerised lists, to prevent selection errors.

The antidiarrhoeal drug eluxadoline has been assigned the common stem -adol-, used to denote analgesics. Unawareness of its pharmacological effect on bowel opioid receptors may lead, according to participants’ advice, to cause confusion and wrong-drug errors during clinical use. This risk of misunderstanding should prompt a particular learning approach of the common stem -adol-, in order to demonstrate its consistency.

**In summary**, our analysis of the INNs proposed in List 109 raises many questions about both INN comprehensibility and the risks of confusion. These issues must be taken into account when educating healthcare professionals about INNs. Having identified these problems, we can anticipate some occasionally complex mechanisms through which errors could arise and consider how best to improve INN differentiation.

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 presented to them as legibly as possible.

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Review prepared and translated by the Prescrire Editorial Staff with the participation of healthcare professionals from the Association Mieux Prescrire.

No conflicts of interest

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