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## Prescrire's contribution to the WHO consultation on List 106 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 (1–4).

**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 (5).

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 public consultations on proposed INNs, in order to identify any risk of confusion during their clinical use (6). The editorial staff of *Prescrire* and members of the not-for-profit organisation Association Mieux Prescrire are participating in this phase of the consultation and have examined List 106 of proposed INNs, which was published in January 2012 (7).

**Our critical analysis of the proposed INNs.** Our analysis of the 57 proposed INNs of List 106 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 (8–12).

*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 16 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 16 contentious INNs whether a simple comment or a formal objection was more appropriate, and listed their arguments.

One INN that was proposed in a previous list, then amended in response to an objection, was also examined: *netazepide* (to replace *sograzepide*, List 101).

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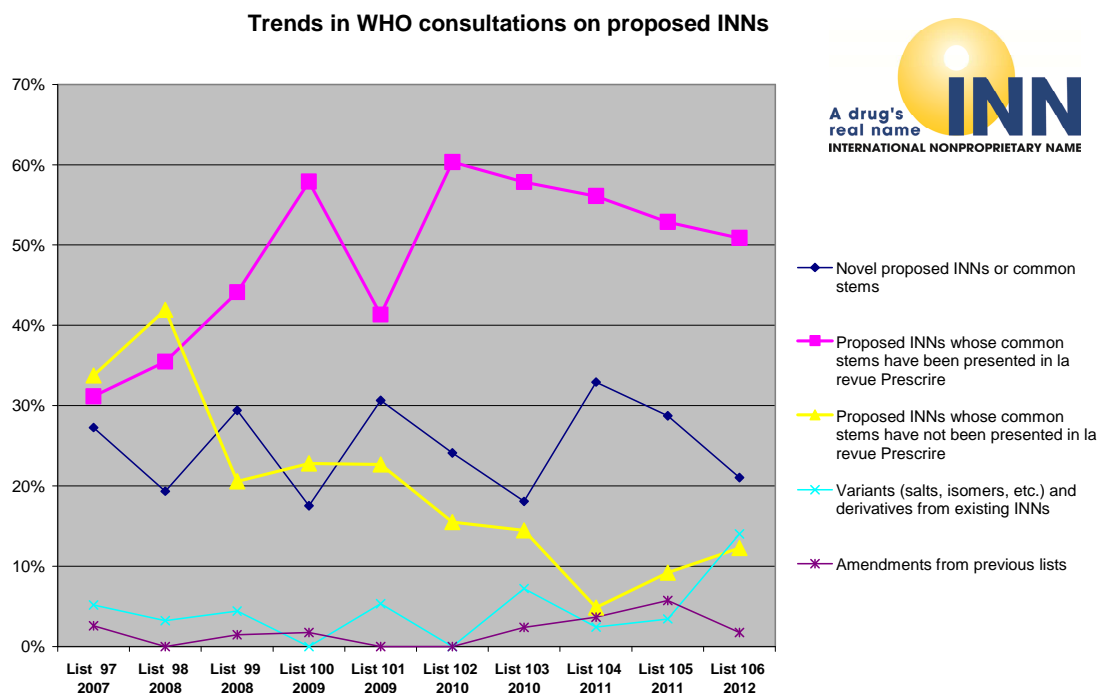
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**No formal objections.** The 57 proposed INNs of List 106 include: 29 proposed INNs whose common stems have been presented in la revue *Prescrire* (51%); 7 proposed INNs whose common stems had not yet been presented in la revue *Prescrire* at the start of our analysis of List 106 (12%); 12 novel proposed INNs or stems (21%); 8 variants, such as salts and isomers (14%); and one amendment to an INN proposed in a previous list. As shown in the graph plotted to monitor *Prescrire's* contributions to consultations on proposed INNs, the pattern of distribution has remained stable, apart from there being more variants in List 106.



The examination of a list of proposed INNs provides an opportunity to discover some pre-stems, of which List 106 includes: **-lisib** (in *buparlisib*) for antineoplastic phosphatidylinositol 3-kinase inhibitors; and **-prazan** (in *vonoprazan*) for proton pump inhibitors not dependent on acid activation, which surprised several participants (7,10). The participants did not identify any serious risks, so no formal objections are being filed.

## Comments

Some proposed INNs generate a risk of medication errors, for a variety of reasons: the sheer number of INNs in certain groups creates similarity; some could be confused with other INNs, particularly if slightly deformed through misspelling, misreading, misremembering or mishearing (termed slips and lapses); some stems are easily confused with other stems; and some INNs can be confused with brand names. Hence the following comments.

**The sheer number of INNs in certain groups creates similarity.** Antineoplastic tyrosine kinase inhibitors are one such group, and the proposed INN *sapitinib* caused some concern.

Similarities were identified between *sapitinib* and *sunitinib*, as well as *lapatinib*. However, in the context of cancer chemotherapy, it is difficult to evaluate the seriousness of a potential mix-up, which would depend on the doses used. One way of amplifying the differences between the INNs of tyrosine kinase inhibitors, of which we have identified 43, would be to highlight the variable portions, excluding the stem **-tinib**, for example with upper-case

lettering (known as Tall Man lettering) (9).

In contrast, none of the 8 INNs for monoclonal antibodies proposed in List 106 warranted comment.

**Risks of confusion with other INNs.** Some proposed INNs, such as *naltalimide*, *ondelopran*, *refametinib* and *sutezolid*, could be confused with other INNs.

*Ondelopran* contains no identifiable stem, and the participants felt that any confusion involving an opioid receptor antagonist could have serious clinical consequences. With this in mind, the risk of erroneously selecting *ondansetron* instead of *ondelopran* from a list on a computer screen should be taken into account when choosing how the drugs are displayed in computerised prescribing software. A visual resemblance between *ondelopran* and *citalopram* was also identified, but the consequences of confusing the two were considered less worrying.

The similarity between *refametinib*, *remifentanil* and *repaglinide* should also be taken into account when analysing the risk of selecting the wrong drug from a computerised list. Tall Man lettering could be used in computerised prescribing systems and on labelling to help highlight the differences between them, e.g. *reFAMEtinib*, *reMifentanil*, *rePAGlinide*.

*Sutezolid* and *budesonide* sound alike in French, since they contain the same sequence of vowels. Although the risk of confusing the two would be mitigated by the expected differences in their formulations and routes of administration, the labelling and package leaflets of marketed products containing these substances would need to be very clear.

Although the potential for confusion between *naltalimide* and *thalidomide* was identified, the risk was considered low because both substances require specific medical supervision.

**Confusions worsened by lapses and slips.** The participants identified certain lapses and slips that could create confusion between INNs, particularly *naltalimide* and *pradigastat*.

Confusion between *naltalimide* and *lenalidomide*, and between *pradigastat* and *dabigatran* were considered potentially dangerous. These risks are a reminder that the effect of dyslexia should not be overlooked in any systematic assessment of the risk of confusion between drug names.

Several factors conspire to create confusion between *pradigastat* and *dabigatran*, increasing the likelihood of mistaking the new INN *pradigastat* for "pradigatran". The –gastat suffix resembles the stem –**g**atran, and the same vowels are present in the same sequence in *dabigatran*, marketed as Pradaxa°. Furthermore, it comes at a time when many healthcare professionals are not yet fully conversant with the host of new oral anticoagulants appearing on the market.

**Risks of confusion between stems.** Some of the proposed INNs could generate errors due to confusion between stems, e.g. *cerlapirdine*.

The suffix –pirdine has already been assigned by the USANC to 5-HT<sub>6</sub> receptor inhibitors, which are used as cognition enhancers, and could be confused with the stem –**dipine** (*lercanidipine*, *nicardipine*) and with the suffix –pridine (*amifampridine*, *fampridine*) which is not a stem. The risk of confusion between the suffixes –pirdine and –pridine is particularly high since they are identical apart from two inverted letters.

Prescrire has already pointed out the risks of confusion associated with the suffix –pirdine, by filing an objection to *latrepirdine* (List 102) due to its similarity to *ticlopidine* (13). These confusions could have clinical consequences that should deter the INN programme from adopting it as a pre-stem.

**Risks of confusion with brand names.** Some proposed INNs resemble existing brand names, creating a risk of medication errors. Confusion between the following proposed INNs and drugs marketed in France were considered particularly dangerous: between *amitifadine* and Rifadine° (*rifampicin*); between *buparlisib* and Buspar° (*buspirone*; withdrawn from the French market); between *lucerastat* and Séresta° (*oxazepam*) or Lucentis° (*ranibizumab*);

and between *tozadenant* and Tadenan° (*Pygeum africanum* extract).

**In summary**, our analysis of List 106 of proposed INNs shows that progress can still be made to improve the safety of INNs and that future common stems should be carefully chosen. In particular it reveals some counterintuitive mechanisms through which errors could arise, which should be carefully taken into account when educating healthcare professionals about INNs. Prescribers and users can only think successfully in terms of INNs when these names are devised and taught in a rigorous and consistent way.



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