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Prescrire's contribution to the WHO consultation on Proposed INN: List 99

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As an active member of the Medicines in Europe Forum and the International Society of Drug Bulletins (ISDB), *Prescrire* has long been advocating the routine use, by both healthcare professionals and patients, of international non proprietary names (INNs), which are clearer and therefore safer than brand names (1-4).

Making INNs safer. The basic principles underlying the selection of individual INNs are the same that apply to the prevention of medication errors, namely standardization, differentiation, redundancy, and built-in logical controls. INNs make pharmaceutical substances easier to identify and are less frequently confused than brand names (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 INN, calls for active participation in public consultations on proposed INNs, within a four-month period of the date of final adoption, in order to review proposed INNs from the perspective of in-use safety (6). *Prescrire* is participating in this phase of the survey and has now examined the List 99 of proposed INNs, published on 1 July 2008 (7).

Critical assessment of proposed INNs. Our analysis of the List 99 of Proposed INNs was based on the 2006 list of common stems and its update, on the Summary List #12 CD-ROM, as well as the INN database, and on a database of drugs marketed in France which provides both trade names and corresponding INNs (8-10). *Prescrire* used a two-step Delphi method. First, *Prescrire* editors compiled a list of potentially litigious proposed INNs, along with the relevant reasons. For each of the 31 proposed INNs selected for further scrutiny in this first step, the editors assessed the risk of confusion and/or misunderstanding, along with the potential clinical consequences of such errors. Finally, they decided whether a simple comment or a formal objection was more appropriate for each litigious INN, and listed their arguments.

Formal objections: inolitazone and tanezumab

Inolitazone is unacceptable. The risk of mistakenly taking inolitazone for a glitazone creates a danger that diabetic patients might receive this antineoplastic drug by error. This risk of confusion was considered serious by the *Prescrire* team, in terms of both its potential frequency and its potential severity; the high toxicity of this antineoplastic drug is such that a formal objection is justified. This proposed INN is doubly unacceptable because it scrambles the meaning of the common stem **-glitazone**, which is now widely recognised and understood. The absence of the letter "g" rules out the notion of antidiabetic treatment, but the difference is too small to avoid the risk of confusion altogether.

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Danger with tanezumab. The common stem **-zumab** designates humanised monoclonal antibodies, generally used as immunomodulators or as antineoplastic drugs. Nothing in the proposed INN tanezumab suggests this drug's analgesic properties. In addition to creating confusion around this common stem, there is an added risk of confusion with other monoclonal antibodies, with potentially serious consequences.

Prescrire considers that a more explicit name should be sought, for reasons of safety and for clearer distinction of monoclonal antibodies used for analgesic purposes. The pharmacological action should be more visible than the monoclonal antibody concept, whose identification, even though it points to properties, is not what matters most to healthcare professionals.

Comments

The following comments concern proposed INNs that might lead to medication errors due to a variety of reasons: some carry a risk of confusion with other INNs or common stems; some undermine acquired knowledge; some could be confused with the names of alkaloids or with brand names used in France; and others seem to be commercially biased.

Risk of confusion with other INNs or common stems. Some proposed INNs, such as elesclomol, tasisulam, and tildipirosin, do not contain a common stem or a newly selected pre-stem (8, 10). Others, especially bevasiranib, danusertib, lancovotide, larazotide and lixisenatide, carry a risk of confusion with other INNs or with other common stems.

Lacking an identifiable common stem, the name elesclomol creates a risk of confusion with INNs comprising a similar portion, such as paracetamol, dipyridamole, salbutamol and trometamol; but, in the absence of more precise information on the properties of elesclomol, it is difficult to appreciate the consequences of this confusion.

The name tasisulam carries a risk of confusion with the common stem **-azolam** used for benzodiazepines not ending in **-azepam**. Although this does not warrant a formal objection, the serious consequences of using an antineoplastic drug instead of a psychotropic warrant re-examination of this proposed INN.

The name tildipirosin does not suggest antibiotic properties, and could be confused with pyridoxine or with alfablockers, the stem **-irosine** being close to **-azosine** (as in alfuzosin, doxazosin, prazosin and terazosin).

Among the proposed INNs ending in **-tide**, the name lancovotide, when written, carries a risk of confusion with enfuvirtide; the same applies to the pairs larazotide-lanreotide, and lixisenatide-exenatide. The very broad range of this stem used for peptides and glycopeptides might increase the risk of confusion between INNs of this type.

A risk of confusion has been identified between the names bevasiranib and bevacizumab, when handwritten, especially as these two drug substances can be used concomitantly in cancer centres. Although not negligible, the risk appears to be lower with danusertib-dasatinib and palifosfamide-palifermine.

Misunderstood proposed INNs: predictable sources of errors. Some INNs contain common stems that may be difficult to identify.

The common stem **-vir-** inserted in the middle of a proposed INN appears more difficult to identify in foravirumab and rafivirumab, because attention is drawn by the common stem **-umab** used in the names of monoclonal antibodies. The pharmacological action should take precedence over the nature of the drug substance, especially as the growing number of INNs reduces the ways of differentiation.

Risk of confusion with an alkaloid name. Denenicokine could be confused with nicotine, an alkaloid and not an INN. *Prescrire* proposes "deneconikine" as an alternative, but has not checked whether this conveys less undesirable connotations in other languages than in French.

Risk of confusion with French brand names. The similarity between edoxaban and Endoxan^o could lead to confusion, exposing a patient simultaneously to the toxicity of cyclophosphamide and to thromboembolism due to a lack of prophylaxis.

Proposed INN with a commercial flavour? Most INNs are proposed by the relevant drug companies, and, as such, are sometimes considered to be a part of an overall commercial strategy. Thus, the proposed INN adaprazine not only recalls niaprazine (a psychotropic suspended then reintroduced in France, branded as Nopron^o) but also contains the stem "ado", suggesting adolescence, at a time when the use of antidepressants by young people is an emerging problem.

Helping to understand INNs

Prescrire's analysis of these proposed INNs also highlighted problems of comprehension.

Distinguishing between true and false common stems. When they are not related to a homogeneous pharmacotherapeutic class, common stems as common as **-ol**, **-tide**, **-oxime**, etc., should be used with care.

The suffix **-ol** can evoke a betablocker, as for example in befiradol, where the common stem **-adol** is specific to analgesics (see also tramadol).

The suffix **-oxime** present in olesoxime was wrongly perceived as a common stem, creating a risk of confusion with other INNs ending in **-oxime**, such as cefmenoxime, cefpodoxime, ceftizoxime and cefuroxime, but also pralidoxime, etc.

The common stem **-tide** is used for many peptides and glycopeptides with a variety of properties, such as disitertide, lancovotide, larazotide and lixisenatide. It appears even more ordinary as this suffix is also present in trade names (for example, in France, Becotide^o, Cetrotide^o, Flixotide^o, Seretide^o, and Vistide^o).

The lack of any logical link between some INNs and their pharmacological properties calls for further verification to avoid errors, and this may warrant specific information being provided to healthcare professionals.

Other pitfalls can be avoided through appropriate education. The problems noted with the common stem **-vi(r)-** inserted in an INN do not only indicate that it is easier to recognise as a suffix. Special efforts may be needed to help identify it, not only in the List 99 of proposed INNs (foravirumab, rafivirumab and tecovirimat; when these substances arrive on the market), but also with already marketed substances (delavirdine, efavirenz, enfuvirtide, etravirine, nevirapine, ribavirin).

Difficulties with some INNs for gene therapy products, although very informative (such as alipogene tiparvovec on List 99), mean that healthcare professionals should receive relevant information when such substances become available.

In summary, in this, its third contribution to a WHO consultation on proposed INNs, *Prescrire* considers that the efforts made by the WHO INN Program must be backed up with specific information and education for healthcare professionals and patients.



Bruno Toussaint
Chief editor

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