Prescrire
83, boulevard Voltaire
75558 PARIS CEDEX 11
FRANCE

Tél. : (33) (0)1 49 23 72 80
Fax : (33) (0)1 48 07 87 32
contact@prescrire.org

Site internet
Web site
www.prescrire.org

Service aux Abonnés
Subscription Department
Tél. : (33) (0)1 49 23 72 86
Fax : (33) (0)1 49 23 76 48
abonnements@prescrire.org

Formations Prescrire
Tél. : (33) (0)1 49 23 72 90
Fax : (33) (0)1 49 23 72 50
formations@prescrire.org

Association Mieux Prescrire

Organisme indépendant
de formation permanente
des soignants

Independent organisation
continuing education
for health professionals

Agréments FMC, EPP et autres
Org. FC 11 751 711 075
N° TVA : FR 48 340647619
SIRET 340 647 619 00014
Code NAF : 9499Z
RIB La Banque Postale Paris :
20041 00001 0061205H020 22
Association loi de 1901
n° 86/4331 - JO 21/01/1987
(Statuts sur demande).

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

Paris, November 12, 2009

Prescrire's contribution to the WHO consultation on List 101 of proposed INNs

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

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 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. 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 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 101 of proposed INNs, published on 15 July 2009 (7).

Our critical analysis of the proposed INNs. Our analysis of List 101 of proposed INNs was based on the 2006 list of common stems and its updates, the INN database, and on a database of drugs marketed in France, which enables searches on both brand names and INNs (8-10).

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 37 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 contentious INN whether a simple comment or a formal objection was more appropriate, and listed their arguments.

Formal objections

A formal objection was deemed necessary for several proposed INNs from List 101, because they were uninformative and did not comply with the usual conventions for developing INNs, which are so important for conveying what a pharmaceutical substance is and does. The INNs concerned are *obeticholic acid*, *albitiazolium bromide*, *arhalofenate*, *enisamium iodide*, *insulin degludec*, *turofexorate isopropyl* and *zauritegrast*.

It is unacceptable that the INNs for the antiviral drug *enisamium iodide* and the antimalarial *albitiazolium bromide* contain no clues about their potential use and at first sight appear to be quaternary ammonium compounds, normally used as antiseptics. Antivirals are expected to contain the common stem **vir**, so its absence from *enisamium iodide* is particularly confusing.

INNs such as *arhalofenate* and *zauritegrast* do not comply with the principles governing the creation of INNs, which state that the letter “h” should be avoided and “au” should be simplified to “o”. More importantly these INNs contain no clues as to their potential use, the first being an antidiabetic and the second a non-steroidal anti-inflammatory drug (see below).

Another particularly disconcerting source of confusion is when very different INNs are used for drugs with the same potential mechanism of action. This is the case for *obeticholic acid* and *isopropyl turofexorate*, which are both listed as “farnesoid X receptor agonists”, acting through a bile salt mechanism that was unfamiliar to the participants in this group analysis. Shouldn’t a new common stem be created when a new mechanism of action is acknowledged?

Finally, with two-word gene therapy products now arriving on the market, the proposed INN *insulin degludec* could be mistaken for such a product, with the second word of this proposed INN being taken for the name of a vector. Furthermore the second word could cause confusion about the route of administration if the substance needs to be injected, because in French *degludec* resembles the word “déglutir”, which means to swallow, suggesting oral administration to some participants.

The potential clinical consequences of the mix-ups or misunderstandings associated with these INNs were deemed sufficiently serious to justify these formal objections. They should prompt the INN programme to re-examine the various inconsistencies identified to prevent potential problems for healthcare professionals and patients in the future.

Other comments

Some proposed INNs generate a theoretical risk of medication errors, for a variety of reasons: some carry a risk of confusion with other INNs, particularly in the case of monoclonal antibodies; some are difficult to understand; some do not correlate with the indications claimed by the pharmaceutical company; and some could be confused with French brand names. Hence the following comments.

Risks of confusion with other INNs. Some proposed INNs such as *aganirsen*, *ataluren*, *miravirsen* and *modithromycin* could be confused with other INNs.

Within List 101 of proposed INNs, the INNs for the angiogenesis inhibitor *aganirsen* and the antiviral *miravirsen* are too similar, and the common stem **vir** that indicates their different pharmacological properties is not conspicuous enough.

Some risk of confusion, albeit minor, was identified by some participants between the 2 antibiotics *modithromycin* and *roxithromycin*; and also between *ataluren* and *aliskiren*.

Dealing with the growing number of monoclonal antibodies. According to our calculation, there are currently 176 INNs for monoclonal antibodies with the common stem **–mab** (9). Whereas they accounted for nearly a quarter of List 100 of proposed INNs (14 out of 57), there are 12 substances of this type among the 75 proposed INNs in List 101: *briakinumab, daratumumab, fezakinumab, fresolimumab, girentuximab, iodine (^{124}I) girentuximab, intetumumab, lebrikizumab, rilotumumab, rontalizumab, sifalimumab* and *teprotumumab* (7,11).

The proliferation of INNs with the common stem **–mab** increases the risk of confusion among pharmaceutical substances based on monoclonal antibodies which are used in very different indications. Most participants were struck by the risk of confusion in both sound and spelling between *fezakinumab* and *fresolimumab* in List 101 of proposed INNs. Information about the sub-stem *–k(i)-*, also present in *lebrikizumab* will help warn *Prescrire*'s subscribers to watch out for this risk of error (12).

Poorly comprehensible proposed INNs: foreseeable problems. Participants noted that some INNs might be difficult to understand because common stems were insufficiently conspicuous and sometimes missing, providing no clues as to their potential use, for example *afacifenacin*, *danegaptide*, *davalintide*, *lomitapide* and *miravirsen* (see above).

Participants unaware of pramlintide did not recognised *davalintide* as an antidiabetic because it does not contain the common stem **gli**, which is usually associated with this therapeutic class. Associated with *insulin* use, the resulting risk of medication error could lead to a hypoglycaemic event.

The absence of common stems identified in some proposed INNs means that their pharmacological properties are not easily identified. Thus, *lomitapide* could be confused with *loperamide*; *danegaptide* sounds to some participants more like an antidiabetic than an antiarrhythmic, and furthermore could be confused with *davalintide* which also features in List 101 of proposed INNs; 2 participants thought that *afacifenacin* sounded like a quinolone.

Arhalofenate is more evocative of an antimalarial or a lipid-lowering fibrate drug than an antidiabetic, and it is far from obvious that *zauralegrast* is a non-steroidal anti-inflammatory drug.

In summary, these conflicts between a proposed INN and the indications claimed by the drug company can lead to failed identification and increase the risk of confusion with other INNs.

Risk of confusion with French brand names. A further risk of confusion was identified in the similarity between *ataluren* and various drug brand names used in France such as Antarène°, Scoburen° and Voltarène°. This risk particularly applies to telephone prescribing and computerised prescribing, when drugs are selected from lists that include both brand names and INNs; examples include *ataluren* and Antarène°, *elisidepsin* and Eldisine°, and several participants noticed a risk of confusion between *turofexorate isopropyl* and Deroxat°.

In summary, most of the proposed INNs from List 101 are acceptable while some need to be revised. After this fifth participation in a WHO consultation, *Prescrire* recognises the efforts made by the WHO INN Programme but considers that specific information and education will be needed, especially in the case of monoclonal antibodies, if healthcare professionals and patients are to adopt the proposed INNs. Prescribers and users can only think in terms of INNs when these names are devised in a rigorous and consistent way.

Bruno Toussaint
Chief editor

Review prepared and translated by the *Prescrire* Editorial Staff with the participation of healthcare professionals from the Association Mieux Prescrire, no conflicts of interest

References

1- Prescrire Rédaction “Prescrire et penser en DCI : une bonne pratique professionnelle” *Rev Prescrire* 2000 ; **20** (209) : 606-623.

2- Prescrire Rédaction “DCI : la priorité” *Rev Prescrire* 2005 ; **25** (265) : 641.

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- Prescrire Rédaction “Confusion entre noms commerciaux : entretenue par les agences du médicament” *Rev Prescrire* 2007 ; **27** (290) : 941-945.

6- Council of Europe - Expert Group on Safe Medication Practices “Creation of a better medication safety culture in Europe: Building up safe medication practices” Version préliminaire du rapport mise en ligne le 19 mars 2007 : 257 pages.

7- OMS “Dénominations communes internationales proposées: Liste 101” *WHO Drug Information* 2009 ; **23** (2) : 129-192.

8- WHO “The use of stems in the selection of International Nonproprietary Names (INN) for pharmaceutical substances” WHO/PHARM S/NOM 15 2006 + Addendums 1 + 2 + 3 + 4; 172+4+4+5+4 pages.

9- WHO “International Nonproprietary Names (INN) for Pharmaceutical Substances” Site mednet.who.int.

10- WHO “Pre-stems: Suffixes used in the selection of INNs March-April 2009” 11 June 2009; 5 pages.

11- OMS “Dénominations communes internationales proposées: Liste 100” *WHO Drug Information* 2008 ; **22** (4) : 311-367.

12- WHO “Nomenclature for monoclonal antibodies” *WHO Drug Information* 2009 ; **23** (3) : 195-199.