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Prescrire's contribution to the WHO consultation on List 124 of proposed INNs (special edition)

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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 escalating number of INNs now in circulation and the sheer number of applications for new INNs, some of which are never used. 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 other contributors, including lecturers in pharmacy and medicine, has examined List 124 – COVID-19 (special edition) in order to participate in the public consultation on this latest list of proposed INNs, published in October 2020 (a)(9).

Our critical analysis of the proposed INNs. Our analysis of the 25 INNs proposed in List 124 was based on the following resources: the WHO's Stem Book 2018 (and its addendum), INN database, and lists of pre-stems, biological and biotechnological substances, and radicals; the United States Adopted Names (USAN) stem list; databases of drugs marketed in France, which enable 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 124. In each case, the participants then assessed the likelihood and clinical consequences of a medication error and/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.

A special COVID list. This special list consists of 25 INNs proposed for drugs intended for the prevention or treatment of infection with the virus SARS-CoV-2.

Our examination of List 124 identified the use of two pre-stems: **-meran** for messenger RNA (mRNA), and **-toran** for Toll-like receptor 4 (TLR4) antagonists (12).

No formal objections. None of the risks of confusion or misunderstanding associated with the INNs proposed in List 124 were of sufficient concern to warrant a formal objection.

Comments

Our review group identified a number of proposed INNs that could generate medication errors, either through confusion with another INN, or due to inadequate regulation of drug brand names by regulators.

Potential confusion with another INN. Some of the INNs proposed in List 124, especially *eclitasertib*, *ganulamieran*, *pidacmeran*, *regdanvimab*, *tozinameran* and *zorecimeran*, could be confused with other proposed or recommended INNs.

The proposed INN *eclitasertib* could be confused with the INN *etelcalcetide*, mainly due to their phonetic resemblance in French, and with *delcasertib*, an INN proposed in List 105 for a drug that has not, to our knowledge, been marketed as yet (19).

A risk of confusion exists between the proposed INN *ganulamieran* and *gindameran*, an INN proposed in List 123, with which it shares 8 letters, in the same order, and overall visual similarity (20). They are especially likely to be confused when selecting drugs from an alphabetical menu.

The proposed INN *pidacmeran* could be confused with *gindameran* too, with which it shares 8 letters in the same order, the same sequence of vowels and the same sequence of descenders and ascenders (20).

The proposed INN *regdanvimab* could be confused with *regavirumab*, an INN proposed in List 80. However, to the best of our knowledge, *regavirumab* has not yet been marketed, making the risk of confusing these two drugs low for the time being (21).

Our review group felt *tozinameran* and *zorecimeran*, both proposed in List 124, to be too similar, both visually and phonetically.

In summary, of the five INNs proposed for mRNA vaccines, and ending therefore in the stem **-meran**, *abdavomeran* seems to be the only one that is not likely to cause confusion.

Potential confusion due to inadequate regulation of drug brand names. The INN *goflikicept*, proposed in List 124, confused one of our reviewers due to the fact that its stem **-cept** is present in Cellcept[®], the brand name of a product that contains *mycophenolate mofetil*. This reviewer mistakenly thought that these two immunomodulators would have the same mechanism of action, which is not the case. This stem is also present in other brand names, including Aricept[®], which contains the cholinesterase inhibitor *donepezil*, a drug with rather different pharmacological properties from those of selective immunosuppressants. This situation contravenes WHO resolutions calling on member states and drug regulatory agencies to protect the integrity of INNs and stems, in order to help prevent any confusion between INNs and brand



names. One WHO resolution, passed in 1993, asks member states to avoid brand names derived from INNs or established stems. However, the reaction of this reviewer is a reminder that regulatory agencies have tolerated drug brand names containing stems (22,23).

In summary. List 124 – COVID-19 (special edition) highlights the swift action taken by the WHO INN programme to make INNs available to healthcare professionals. This remarkable effort enables health professionals to make independent treatment choices, focusing on what really matters: first the choice of drug, then the dose and the pharmaceutical form. It also informs them of the drugs' therapeutic class or/and mechanism of action, and therefore about their expected adverse effects and interactions.

It is a shame that INNs are not always used when drugs first appear on the market, even in an emergency. The use of codenames alone to refer to certain messenger RNA vaccines is a recent example of this, and a missed opportunity. We note too the EMA's inconsistent use of the INN of the first COVID-19 vaccine (*tozinameran*) to receive conditional authorisation, indicating the European authorities' lack of trust in or respect for the use of INNs, and making it all the more difficult for European citizens to clearly distinguish between these vaccines without resorting to the use of their brand names.

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Publishing Director

**Review produced collectively by the *Prescrire* Editorial Staff:
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a- This response was prepared using the resources of the entire Prescrire team. Head of team analysis and preparation: Éric Bel (pharmacist). The members of the Prescrire editorial team who made a particular contribution to this review were Anne Americh (pharmacist), Élodie Artielle-Beaucamp (pharmacist), Christine Guilbaud (pharmacist), Mélanie Hardy (pharmacist), Sébastien Hardy (pharmacist), Fabienne Jourdan (doctor), Laurence Le Quang Trieu (pharmacist), Florent Macé (pharmacist), and Étienne Schmitt (pharmacist). The other contributors were Imene Beghriche (pharmacologist), Jacques Cogitore (doctor), and Helen Geneviev (translator).

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