

Drug packaging: still too many problems in 2003

All factors contributing to the poor use of drugs or influencing the risk-benefit ratio of a given treatment must be examined, and this includes packaging components such as bottles, blister packs, stoppers, information leaflets, and delivery accessories (1-5).

La revue Prescrire has always paid special attention to the quality of drug packaging, and for several years a specialised team has examined in detail the packaging of all pharmaceuticals appraised in the New Products column (1). The team examined the packaging of more than 400 different products in 2003, and a number of trends emerged.

Tablets and capsules: inadequate blister labelling. 90% of the tablets and capsules we examined in 2003 were sold in blister packs. The unit-doses [each separate blister] were not individually labelled in 96% of packs, creating the risk of confusion when the tablets or capsules are removed (a,b). Just a few tablets and capsules were printed with identifiers that could be recognised by the patient (c,d), and half of blisters that did were barely legible (e).

10% of the tablets and capsules examined in 2003 were sold in bulk bottles, usually without a safety stopper. This increases the risk of massive overdose, both accidental and deliberate, especially by children.

Oral formulations: risky dosing dispensers. Oral formulations represented 8% of new products released in 2003. Most bottles contained multiple doses, yet virtually none had safety caps, including products with attractive aromas for use in children (e.g. Toplexil°, oxomemazine, see French edition n° 245 p. 829).

Some dosing dispensers did not carry the INN or trade name, exposing patients further to the risk of drug errors

if two medicines with dispensers are inadvertently exchanged. Other dispensers were graduated imprecisely or illegibly, such as the graduated spoons provided with amoxicillin bottles in France. Simple dosing cups were still being provided with products released in 2003, once again increasing the risk of overdose (f).

Unit-dose sachets, which allow clear labelling, were used for only 3.4% of new oral formulations released in 2003.

Rare improvements for injectable preparations. Improvements noted in 2003 included ready-to-use infusion bags and prefilled syringes (g). Yet 63% of products were sold in simple bottles or vials, with no devices for preparation or injection. Some vials contained multiple doses, increasing the risk of infection when several patients are treated from the same bottle (h).

The packaging of some injectable preparations, such as Copaxone° (glatiramer, see *Prescrire International* n° 69 on page 10), is well designed, but patients have to be taught by nurses how to use the delivery devices. This may be acceptable for useful drugs, but certainly not for medicines providing no tangible benefits. And is the extra workload for nurses taken into account when deciding the price of such preparations?

It's time for health professionals to react. Comparative evaluation of all packaging for old and new drugs in 2003 identified other problems: the potential for drug errors due to the poor choice of colour and graphics on boxes, the international non proprietary name (INN) printed in tiny lettering while the trade name stands out clearly, and patient information leaflets that are user-unfriendly, too technical or inconsistent.



1- Hey! look at the nice little box
Piss off!
Licensing body

2- We got the licence
Pretty box, isn't it?
Piss off!
Whatsit & co®

3- Gee! they don't give a shit!
Clinical practice

Prescrire International translation procedures

Team work and strict quality control procedures

The situation is as worrying for originator drugs as for generics. And our long-term monitoring shows that no progress has been made over the years.

Given the apparent lack of reaction of the French medicines agency, and the lack of precise packaging quality standards in Europe, health professionals should report all packaging problems to the authorities and the companies concerned (with copy to *la revue Prescrire*).

Prescribers, pharmacists and nursing staff should also create quality groups, in order to share their experiences and to choose the drugs best adapted to each category of patients (6).

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a- The Prescrire editorial team defines unit-dose blisters as those bearing on the back of each individual blister the INN, the dosage, the batch number and the expiry date. In 2003, examples of such blisters in France included Thalidomide Laphal[®] (thalidomide, see *Prescrire International* n° 67, p.165) and Fluiumucil[®] effervescent tablets (acetylcysteine, see French edition n° 242, p. 587). Around 7% of blister packs examined in 2003 bore the INN and unit dose but not the batch number or the expiry date.

b- For patient-named delivery in hospitals, the pharmacy staff has to take all the tablets or capsules out of the blister packaging, and label those that are not properly labelled, individually for use on the ward.

c- The Prescrire editorial team consider that a unit-dose is in France identifiable when it bears the trade name or INN (printed or engraved). Good examples include Advil[®] 100 mg (ibuprofen, see French edition n° 238, p. 264) and Zovirax[®] 200 mg (acyclovir, see French edition n° 244, p. 736). Yet 70% of unit-doses studied in 2003 carried no label, and 30% only carried a manufacturing code.

d- In 2003 the Prescrire editorial team noticed a trend towards the use of fragile orally fast-dissolving tablets (Zydis[®]). These disintegrate almost immediately in mouth, without water, a property which can be helpful in some circumstances. The SPC for Zyprexa Velotab[®] (olanzapine, see French edition n° 239, p. 336), recommends that the tablets be kept in their blisters until use, and the blisters are thus individually labelled. This is not the case for Imos-sellingual[®] (loperamide, see French edition n° 245, p. 824).

e- Several factors can make the printing on a blister illegible, such as the use of small characters, poor colour choice, cramped information, shiny material. Poor examples in 2003 include the Bacterix[®] blister pack (nifuroxazide, see French edition n° 242, p. 586), on which the labelling is difficult to read and does not mention the INN (even though the trade name wrongly suggests antibiotic effects); and the poorly legible blister packs of Ebixa[®] (mefenazine, see *Prescrire International* n° 68, p. 203), a drug used for Alzheimer's disease.

f- In 2003, Deroxat[®] oral solution (paroxetine, see French edition n° 237, p. 167-170) still has a dosing cup. They were given a Prescrire Red Card for this poor packaging in 2000 (*Prescrire International* n° 52, p. 35).

g- For example, glucagon is sold as a syringe prefilled with solvent + a vial of powder in a rigid box containing illustrated directions for use (Glucagen Kit[®], see French edition n° 245, p. 824); dobutamine is sold in ready-to-use sachets (Dobutamine Baxter[®], see French edition n° 244, p. 739) (note, however, the poor choice of a sulfite preservative which can cause severe allergic reactions); and the new packaging of Avonex[®] in prefilled syringes (interferon beta-1a, see French edition n° 245, p. 814).

h- Examples include Tubertest[®] (tuberculin, see French edition n° 243, p. 665-666), and Vistabel[®] (type A botulinum toxin, see *Prescrire International* n° 67, p. 180).

1- Prescrire Editorial Staff "Drug packaging: safety and convenience above all" *Prescrire Int* 2002; **11** (57): 26-27.

2- Prescrire Rédaction "Intrarachidiennes et épidurales: des voies d'administration à haut risque" *Rev Prescrire* 2003; **23** (242): 591-602.

3- Prescrire Rédaction "Méthotrexate: gare au surdosage" *Rev Prescrire* 2002; **22** (232): 665.

4- Prescrire Editorial Staff "Fatal acute iron intoxication" *Prescrire Int* 2003; **12** (65): 101-102.

5- Prescrire Rédaction "Tirer les leçons d'un conditionnement mal conçu" *Rev Prescrire* 2001; **21** (219): 505.

6- Prescrire Rédaction "Cercles de qualité: des médecins et pharmaciens suisses ouvrent la voie" *Rev Prescrire* 2000; **20** (203): 146-148.

The translation process

Prescrire International is a bimonthly English-language journal containing translations of selected articles from the monthly French edition, *la revue Prescrire*. The international edition was created with two principal aims: first, to offer non French speakers access to *Prescrire's* systematic assessments of health technologies, and especially medicines; and second, to provide a platform for texts dealing with European and other international medicines policies.

The articles to be translated and the content of each issue of *Prescrire International* are chosen jointly by the editor-in-chief of *Prescrire International* and members of the editorial team of *la revue Prescrire*.

The texts are first prepared by a professional translation team, and are then thoroughly verified by a painstaking quality control procedure.

The translation team. The initial translations are prepared jointly by a British translator and the bilingual editor-in-chief of *Prescrire International*, who have both held their positions since the Journal was created in 1992.

The translation team also includes a bilingual editorial assistant responsible for the overall translation process; a British medical editor dealing with style matters; a French editor of *la revue Prescrire* who checks all the translations; the relevant authors and section editors, who approve the translations of their texts; and a British proofreader who checks the translations for typographic errors prior to publication.

The French texts are translated into English by the permanent translator, and checked for accuracy by the editor-in-chief of *Prescrire International*. Each translation is then sent to a British medical editor, who checks the style and looks for ambiguity and inconsistency. Her recommendations are taken into account by the editor-in-chief of *Prescrire International*, who deals with possible ambiguities and accepts or rejects the proposed changes.

The translation is then passed on to the editor with overall responsibility for the initial text, and to the relevant section editor of *la revue Prescrire*. It is also verified by the *Prescrire* desk editor. It is important to note that the responsible editor and section editor also check that the texts remain up to date. Indeed, several months can pass between the final literature update for the original article, publication of the French text, and its translation and publication in *Prescrire International*. Publication of new data can require the English translation to be modified or even cancelled. The date of publication in *la revue Prescrire* (given in the header of each article published in *Prescrire International*), and the date of the last literature update (given in the *Literature search* section at the end of each article) indicate the temporal validity of the English text.

The texts are then page-set by the production team of *Association Mieux Prescrire* (owner-publisher of *Prescrire International* and *la revue Prescrire*), under the responsibility of the editorial assistant. The consistency of the final layout is checked by the editor-in-chief of *Prescrire International*.

The proofs of the entire ►►