Drug packaging in 2008: not enough progress

Among the packaging systems that Prescrire analysed in 2008, very few met all of our quality criteria. Unsuitable packaging, which could put patients at risk, is often the result of choices made by manufacturers.

The risk of error is higher in certain products intended for self-medication, children, partially sighted patients, pregnant women, use in hospitals and other institutions.

There are even some rather disturbing trends: labelling of blister packs that sacrifices the legibility of the international nonproprietary names (INNs) for the sake of multilingualism, excerpts from the package leaflet printed on the back of the box.

We found improvements in many packaging items again this year: this should motivate health professionals concerned about high-quality care to choose the better ones and to push for more progress.

In 2007, the Prescrire packaging workshop noted an overall improvement in the packaging for drugs marketed in France (1).

What was the verdict for 2008?

Not enough progress. The packaging that Prescrire analysed in 2008 satisfies regulatory requirements. However, packaging design sometimes does not adequately take into account quality of care and patient safety. Packaging very rarely met all of our quality criteria (see the 2008 Packaging Awards in April 2009 issue). Yet again, drug packaging in 2008 reflects the fact that manufacturers are making the same old choices:

- labelling that emphasises commercial details (the invented name, company graphics and logos) instead of information that is useful for patient care. The international nonproprietary name (INN) is often less prominently displayed, particularly on blister packs.
- ambiguous labelling of the concentration for injectable drugs (oxycodeone-Oxynorm® la revue Prescrire 291; tamoxifene-NiQuitin® la revue Prescrire 301);
- problems with devices used for dose preparation: no dosing device provided (destromethorphan-Vicks toux sèche miel® la revue Prescrire 299; mecasermin-Inrecel®, this issue p.111); inappropriate dosing devices, such as those graduated in ml rather than in mg for the active ingredient (fosamprenavir-Telzir® oral suspension la revue Prescrire 295; hydroxyzine-Atarax® syrup la revue Prescrire 291); complex dosing devices, such as the fentanyl-Ionsys® ionophoretic transdermal device, which was withdrawn from the market shortly after its introduction (this issue page 110); absence of a safety cap on bottles containing dangerous substances: for example, an easy-to-open cap for a product containing sufficient doses of quinine to be fatal for a child (quinine-crateagus (dry Hawthorn extract)-Okimus® la revue Prescrire 297);
- package leaflets that lack details (levothyroxine L-Thyroxine Serb® la revue Prescrire 299) or that are overly complex (urokinase-Actifed Allergie Cétirizine® la revue Prescrire 296; illegible INN on blister packs; pholcodine-Valda tous sèche sans sucre® and paracetamol-pseudoephedrine-vitamin C-Valda Rhume® la revue Prescrire 302: trivialisation of the risks by the use of herbal medicine labelling);
- unsuitable for women of child-bearing age (ambiguous information in package leaflets about the risks of non-steroidal antiinflammatory drugs (NSAIDs) during the first trimester of pregnancy (ibuprofen-Advilcaps® and Adviltab® Prescrire International n° 100)) (2).

New concerns. A worsening trend in 2008: several cases in which the labelling spans more than one unit dose and is particularly difficult to read. Particulars are printed in several language and in small, thick lettering, sacrificing the legibility of the INN in favour of multilingualism, for marginal savings in manufacturing costs (18 languages with sitagliptin-Januvia® la revue Prescrire 295 and sitagliptin-Xellevia® la revue Prescrire 299; 13 languages for duloxetine-Cymbalta® the revue Prescrire 300). Another striking observation: dangerous statements or illustrations were found in some package leaflets. In addition to the examples mentioned above for some self-medication products and the fentanyl-Durogesic® patch, a misleadingly reassuring statement minimises the adverse effects of nilotinib-Tasigna®: “most of the side effects are mild to moderate and will
generally disappear after a few days to a few weeks of treatment" (3).

Another trend was confirmed: blister packs in which the labelling that specifies the daily dose spans a group of 2 to 4 unit doses (ivabradine-Procoralan® la revue Prescrire 292). This type of labelling could lead to a 2- to 4-fold overdose.

Another practice that could lead to confusion: excerpts from the package leaflet that are printed on the back of the box for certain prescription drugs (risdrozonic acid-calcium-colecalciferol-Actonel Combi® la revue Prescrire 293; ethinyloestradiol-dospirenone-Jasminelle continu® la revue Prescrire 300). Spreading drug information around on different parts of the packaging creates a risk that the package leaflet will not be read in its entirety. Some of these boxes come in the form of a "wallet" (3 folding flaps which act as both box and blister pack), for example Jasminelle® and Jasminellecontinu®. As the package leaflet cannot be placed inside the wallet for these two products, cellophane wrap holds the leaflet and the wallet together. Once the cellophane has been removed, there is a high risk that the package leaflet will be lost (a).

Some positive trends nevertheless. Fortunately, some manufacturers have made good choices, such as packaging systems that have been correctly designed from the beginning (insulín detemir-Levemin® Innulet® la revue Prescrire 294; methadone-Méthadone AP-HP® capsules Prescrire International 99; exenatide-Byetta® la revue Prescrire 295). There are some very rare examples where all of our packaging quality criteria have been met (methadone-Méthadone AP-HP® and miltefosine-Miltex®, see Prescrire International 100).

A few packaging systems which initially had a rather unsatisfactory administration device have been improved (meningoccéal C vaccine-Meningitec® la revue Prescrire 293; rotavirus vaccine-Rotarix® la revue Prescrire 296; epoetin alfa-Eprex® la revue Prescrire 302; risperidone-Risperdalconsta® LP la revue Prescrire 302). There were also examples where ambiguous labelling of drug concentrations has been clarified (levetiracetam for injection-Keppra® la revue Prescrire 304; lopinavir-Ritonavir-Kaletra® la revue Prescrire 291).

Some packaging for drugs that were initially restricted to hospital use and later became available in retail pharmacies were adapted appropriately (onnidazole-Tiberal® la revue Prescrire 297: single-dose blister packs; idarubicin-Zavedos® la revue Prescrire 291: single-dose bottles with child-proof caps; miltefosine-Miltex® la revue Prescrire 300 and Prescrire International 100 p 82).

The progress that was noted in 2007 for the patient information leaflets of drugs licensed through the European centralised procedure has been maintained, probably due to their evaluation by patients. Several package leaflets provide more detailed information to patients and caregivers concerning drug disposal (papillomavirus types 16, 18 vaccine-Cervarix® la revue Prescrire 292). Other package leaflets mention brand names currently used in other European member states. This may help minimise confusion for patients who buy their prescription drugs in another European country, but it does not mean that the INN can be left off the primary packaging (timolol-Geltilm LP® la revue Prescrire 292).

Access to Braille has expanded and many package leaflets refer to the French association Handicapzéro, which supplies package leaflets and labels in Braille. This improvement should become more widespread in 2009.

In practice: keep up the pressure. In the 28 years that Prescrire has been evaluating drug packaging, one has to admit that examples of high-quality packaging have been rare.

Healthcare professionals and patients therefore need to continue to remain vigilant and to maintain the pressure so that manufacturers improve the quality of their packaging for drugs and devices. Health authorities also need to demand higher standards.

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Selected references from Prescrire’s literature search.
3- Commission européenne “Notice-Tasigna (nilotinib)” 19 November 2007; 8 pages.

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