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. Prescrire 2009; 29 (304): 144-145.

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 (montelukast-Singularâ la revue Prescrire 295; pseudoephedrine-cetirizine-Humex Rhinite Allergiqueâ la revue Prescrire 295; rizatriptan-Maxaltâ la revue Prescrire 300). Occasionally the INN is not even printed on the blister pack (ketoconazole/Zaditenâ capsules la revue Prescrire 297; ambroxol-Lysopadolâ Prescrire International 100). The INN is not printed on the external surface of some transdermal patches, which means they cannot be identified once they are applied to the skin (testosterone-Testopatchâ la revue Prescrire 293; nicotin-Niquitinâ la revue Prescrire 301);
- ambiguous labelling of the concentration for injectable drugs (oxycode-Oxynormâ la revue Prescrire 291; tensirolimus-Toriselâ la revue Prescrire 297);
- problems with devices used for dose preparation: no dosing device provided (dextromethorphan-Vicks toux sèche mielâ la revue Prescrire 299; mecamertin-Increlexâ, this issue p.111); inappropriate dosing devices, such as those graduated in ml rather than in mg for the active ingredient (fosamprenavir-Telzirâ oral suspension la revue Prescrire 295; hydroxyzine-Ataraxâ syrup la revue Prescrire 291); complex dosing devices, such as the fentanyl-Ionsysâ iontophoretic 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)-Okimusâ la revue Prescrire 297);
- package leaflets that lack details (levothyroxine L-Thyroxine Serbâ la revue Prescrire 299) or that are overly complex (urokinase-Actosolvâ, this issue p.118). These drawbacks can lead to confusion between drugs, errors during dose preparation or even accidental poisoning (1).

Packaging unsuitable for at-risk patients. Sometimes packaging is inappropriate for particular patient populations, certain types of therapy or the method of supply:
- unsuitable for children (dangerous illustration on the package leaflet showing the administration of fentanyl-Durogesicâ la revue Prescrire 292; inappropriate dose strength for succimer-Succicapitalâ la revue Prescrire 292);
- unsuitable for blind or partially sighted patients (la revue Prescrire 304);
- unsuitable for therapy that requires the use of single-dose units, particularly in hospitals or other institutions (la revue Prescrire 296; la revue Prescrire 297);
- unsuitable for self-medication (la revue Prescrire 295; cetirizine-Actifed Allergie Cétirizineâ la revue Prescrire 296; illegible INN on blister packs; pholcodine-Valda toux sèche sans sucreâ and paracetaol-pseudoephedrine-vitamin C-Valda Rhumeâ 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-Advilcapsâ and Adviltabâ 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-Januviaâ la revue Prescrire 295 and sitagliptin-Xeleviaâ la revue Prescrire 299; 13 languages for duloxetine-Cymbaltaâ la 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-Durogesicâ patch, a misleadingly reassuring statement minimises the adverse effects of nilotinib-Tasignaâ: “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 (rise-dronic acid-calcium-colecalciferol-Actonel Combîâ la revue Prescrire 293; ethinyleradiol-drospirenone-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 (insulin detemir-Levemir° Innolet° insulin detemir from the beginning - systems that have been correctly designed. The priorities, particularly in poor countries, are to enforce stricter regulation of the legal drug products, legal drug copies (including generics) and parallel imports.

A few packaging systems which initially had a rather unsatisfactory administration device have been improved (meningococal 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 (orindazole-Tiberal° la revue Prescrire 297: single-dose blister packs; ilarabiniv-Zavedos° la revue Prescrire 291: single-dose bottles with child-proof caps; miltefosine-Miltelex° 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-Geltim° 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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