Drug packaging in Europe: what factors drive progress?

A number of measures and guidelines have been introduced in Europe and France to improve the safety of drug packaging.

Progress arising from European guidelines. The implementation of a new European pharmaceutical directive in late 2005 improved the regulatory framework and guidelines in the EU, making medicines safer (1,2). Their impact on drug packaging was an improvement in the quality of the labelling of many new drugs, which prominently display the international nonproprietary names (INNs) of the active ingredients, and an improvement of patient leaflets through the introduction of readability testing.

In 2007, the European Medicines Agency (EMA) announced that it had strengthened its procedure for checking the labelling on packaging items before drugs are introduced to the market (3). The publication of a Council of Europe report in 2006 also provided a strong incentive for the EMA to recognise the importance of medication errors and their prevention (4). The EMA published a guideline on this topic in 2015, following a public consultation launched in 2013 (5).

In practice, drug regulatory agencies set the bar too low. Judging by the marketing authorisations which the EMA grants for oral drugs supplied in bulk bottles or with patient leaflets that lack important safety information, this agency does not take these positive developments sufficiently into account (6).

The same can be said for the French Health Products Agency (ANSM). Many drugs are authorised despite dangerous packaging flaws: labelling that trivialises important information for the prevention of medication errors, such as the INN, poor-quality dosing devices, and patient leaflets that lack important information present in the documentation intended for health professionals or with limited information about excipients. What's more, umbrella brands include drugs bearing the same easy-to-remember brand name but containing different active ingredients (7-10).

The ANSM has made some progress since 2015, issuing some much-needed recommendations that will greatly increase patient safety if put into practice: withdrawing umbrella brands, giving due prominence to INNs, and encouraging the use of unit-dose blisters and accurate dosing devices (6-9).

Progress driven by civil society. The progress made in Europe in the 2000s owes much to the work of the Medicines in Europe Forum, composed of organisations representing patients, consumers, mutual health insurance providers, and health professionals, including *Prescrire* (1). This progress is also due to the regular participation of various organisations in public consultations on drug packaging organised by drug regulatory agencies. The International Medication Safety Network (IMSN) and *Prescrire* contributed in this way to the ANSM recommendations in favour of the prohibition of umbrella brands in France in 2018 (1,6-16).

Campaigning of a French support group (Apesac) for the parents of children with birth defects caused by *valproic acid* played a major role in the introduction of a warning pictogram on boxes of drugs known to be dangerous during pregnancy in France in 2017 (17).

The patient leaflet for the HIV testing device Autotest VIH° shows the exceptional quality that can be achieved when patient organisations are involved, while the packaging of a similar device (Insti°), designed without the collaboration of patients, has many shortcomings (18,19).

Remain proactive. Healthcare professionals and patients also have a very important role to play by reporting packaging flaws that caused or could potentially cause medication errors. In 2017, several French hospital-based healthcare professionals reported the potential for error associated with the coexistence of dosing devices marked with different graduation scales for Haldol° oral solution (*haloperidol*).

1- Prescrire Editorial Staff "Medicines in Europe : citizens' success" *Prescrire Int* 2004; **13** (72): 158/1-158/8.

2- European Commission "Guideline on the readability of the labelling and package leaflet of medicinal products for human use, revision 1" 12 January 2009: 27 pages.

3- European Medicines Agency "Checking process of mock-ups and specimens of outer/immediate labelling and package leaflets of human medicinal products in the centralised procedure" 5 August 2014: 19 pages.

4- Council of Europe - Expert Group on Safe Medication Practices "Creation of a better medication safety culture in Europe: Building up safe medication practices" 2006: 275 pages.

5- European Medicines Agency "Good practice guide on risk minimisation and prevention of medication errors" 18 November 2015: 41 pages.

6- Prescrire Rédaction "Projet de l'ANSM de recommandations sur les étiquetages des formes orales solides: un premier pas encourageant vers plus de sécurisation de l'usage des médicaments, à optimiser" 12 November 2017: 8 pages.

7- Prescrire Editorial Staff "The proposed recommendations on drug brand names by France's Health Products Agency: a plan that maintains dangerous name confusion" 14 December 2016: 4 pages. english.prescrire.org.

8- ANSM "Nom des médicaments - Recommandation à l'attention des demandeurs et titulaires d'autorisations de mise sur le marché et d'enregistrements" January 2018: 9 pages.

10- Prescrire Editorial Staff "Prescrire's response to the European Commission's public consultation concerning its proposed revision of the Guideline "Excipients in the labelling and package leaflet of medicinal products for human use"" 19 May 2017: 4 pages.

11- International Network of Safe Medication Practice Centres (INSMPC) "Unit-dose packaging of pharmaceutical products: comments of the International Network of Safe Medication Practice Centres on French Health Products Safety Agency specifications draft" October 2007: 5 pages.

12- International Medication Safety Network - IMSN "Position statement. Making medicines naming, labeling and packaging safer" 2013: 11 pages.

13- International Medication Safety Network "IMSN encourages regulators and companies to improve medication safety at the global level" Press release, 21 November 2016: 2 pages.

14- Prescrire Editorial Staff "Prescrire's comments on QRD recommendations EMEA/208304/2009. Preventing errors related to the expression of strength on drug packaging" 28 May 2009: 9 pages.

15- Prescrire Editorial Staff "Prescrire's response to the public consultation on EMA/275297/2010 "Draft - QRD recommendations on pack design and labelling for centrally authorised non-prescription human medicinal products" 29 June 2011/ 5 pages. english.prescrire.org

16- Prescrire Editorial Staff "Prescrire's response to the public consultation on EMA/CHMP/QWP/180157/2011 "Draft - Guideline on Pharmaceutical Development of Medicines for Paediatric Use": a pragmatic overview and 20 constructive proposals" 29 December 2011: 20 pages. english.prescrire.org

17- Prescrire Rédaction "Un pictogramme sur les boîtes de médicaments tératogènes ou fœtotoxiques" *Rev Prescrire* 2017; **37** (410): 903-904.

18- AAZ "Notice-Autotest VIH". www.autotest-sante.com accessed 23 January 2017: 2 pages.

19- Prescrire Rédaction "Insti°: deuxième autotest du HIV commercialisé en officine" *Rev Prescrire* 2017; **37** (404): 421.