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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".

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(Statuts sur demande)

Paris, 29 June 2011

Dear Sir or Madam,

In 2011, the European Medicines Agency (EMA) released draft recommendations for public consultation on the packaging of centrally authorised non-prescription drugs, which particularly addressed their labelling (1).

The opinion of the *Prescrire* team on these draft recommendations is presented below, and the points made are developed in and supported by the appended references (2–14).

Summary:

The EMA and the European Commission need to rethink the regulations governing self-medication and safe, easy-to-use medicines. This consultation does not go far enough, as it seeks to accommodate the pharmaceutical companies.

European patients expect high quality healthcare, and the EMA therefore has a duty to show an interest in the packaging of non-prescription drugs used to treat common conditions ("self-medication products"). The quality and rational use of these drugs must take priority, and the packaging of self-medication products must not be allowed to be used to display promotional messages or as children's toys.

But the nature and scope of the QRD Working Group's recommendations, which have been under consultation since March 2011, are insufficient. These recommendations stand little chance of being useful to European patients until they are accompanied by:

1) A policy on self-medication that focuses on the needs and health of European populations, giving priority to the safe naming of drugs, with the international nonproprietary names (INNs) being prominently displayed on the packaging; by prohibiting umbrella brand names and ensuring that dose strengths and concentrations are not expressed in a way that endangers patient safety;

2) Closer monitoring by the European Commission and agencies responsible for drug safety (both centralised and national) to ensure that the current provisions of the European Directive on high-quality packaging design are interpreted optimally;

3) A Directive or Regulation to raise packaging standards, which are currently too lax, to the level required for quality care (15), including in particular:
- extending readability testing and user testing to all the information displayed on all packaging articles (including dosing devices);
- strengthening the evaluation of packaging by drug regulatory agencies (both centralised and national); adding colour mock-ups of the immediate and outer packaging and package leaflets to marketing authorisation (MA) annexes (for new authorisations and major variations); systematically adding a detailed diagram of dosing devices to SPCs and package leaflets (together with precise instructions for their use).

Introduction:

Prescrire, whose aim is to contribute in various ways to increasing the quality and safety of healthcare, regularly points out the great importance of high-quality drug packaging (2–12). *Prescrire*'s expertise is based on its 30-year experience in analysing the packaging of over 5000 medicinal products and in publishing reviews on the subject (2–12).

Prescrire's systematic analysis of drug packaging items regularly prompts it to express concern over their poor quality. This failure to meet quality standards is the root cause of many medication errors, resulting in sometimes serious incidents, some involving self-medication products (2–15). Yet analysis of marketed drugs and drug packaging shows that high quality is possible.

Substandard drug packaging results from flexible or lax interpretation of the provisions of Directive 2001/83/EC on labelling (16,17). The 2009 guidelines on the readability of labelling and package leaflets include some positive points (18), but *Prescrire*'s latest reviews show that they are not often applied (3,4). In particular, it is extremely rare to see labelling that displays the international nonproprietary name of the active substance(s) more prominently than the brand name. The progress brought about by Directive 2004/27/EC, which imposed readability testing for package leaflets, is mainly seen in the quality of centrally authorised package leaflets, yet it should have benefited all drugs in Europe, regardless of the agency that authorised them.

Prescrire's reviews on inferior and dangerous packaging often point out the poor quality packaging of self-medication products: look-alike packaging that is compounded by sound-alike umbrella brand names; company graphics that accentuate these similarities; dose strengths expressed in ambiguous ways; information on blister strips that is hard to read. And of course dosing devices, which are central to the ease of use and safety of liquid multidose forms, are all too often inaccurate, unsuitable or even absent (2–12). The recent review by the Food and Drug Administration (FDA) of the dosing devices of many self-medication products is enlightening and the ensuing FDA recommendations are worth noting (19,20).

As regards package leaflets, according to *Prescrire*'s reviews, the requirement for readability testing has not had a noticeable impact on the quality of the information provided inside the packaging of self-medication products. In France, as in other Member States, many self-medication products were originally authorised through a national procedure and their package leaflets follow a national format. Recommendations focused solely on centralised MAs, however pertinent they may be, will have a very minor impact on the everyday life of European citizens.

The EMA consultation reveals insufficient regulation of self-medication products in Europe.

Against this backdrop, the EMA's approach in adopting such a draft from the QRD Working Group lacks coherence and is insufficient without an appropriate framework (1). Although the EMA's detailed overview of the various self-medication markets in the European Union has not been made publicly available, these markets do not appear so different as far as packaging is concerned. The regulatory requirements for distinguishing between labelling information specific to different Member States are weak (21). However, the list of drugs that are eligible for use in self-medication differs from one State to another (http://www.aesgp.be). For example, at the beginning of 2010, France refused to authorise *sumatriptan* for self-medication of migraine, whereas in the United Kingdom it has been available over the counter since 2006. These differences reflect the absence of a harmonised policy on the authorisation of self-medication products.

The European Commission needs to broaden the scope of the regulation of self-medication products.

Rather than trying to reconcile differences within a working group, it would be better to build the foundation of a self-medication policy in the European Union that is primarily concerned with patients' interest, based on a specific Directive on self-medication or a Regulation if we want to steer European Union Member States closer towards harmonisation (following the lead of the procedures for paediatric drugs).

Prescrire proposes that each self-medication situation (active substance/indication) should be submitted to a specialised EMA group for a centralised opinion; that, prior to marketing, guidelines should be drawn up on each active substance/indication pair authorised by the EMA (following the lead of the procedures for biosimilar products); and that these guidelines should include recommendations on packaging features.

Such a Directive would cover all aspects of drug naming and packaging, particularly for self-medication products, and raise quality standards to at least the level of the recommendations issued by the Council of Europe in 2006 (15). It should address:

- the choice of brand names, because the current European Community guidelines still expose patients to risks (14,17). In particular, *Prescrire* requests a strict ban on the use of umbrella brand names in the European Union, which cause serious mix-ups and medication errors;

- rules on displaying the information that is useful for patient care, adopting the positive points from the guidelines on the readability of labelling and package leaflets, such as: prominently displaying the international nonproprietary name of the active substance(s) (on all the sides of the box) and the excipients; standardising the way dose strengths and concentrations are expressed, in order to prevent medication errors, because in practice the current rules expose patients to too many dangers (see our response to the consultation on this subject in 2009) (13,22);

- rules on the use of colour on drug packaging: *Prescrire* proposes that the EMA schedule a consultation on the use of colour on packaging to improve quality of care, including the use of company graphics, following the lead of the FDA's procedure of 2005 (23), taking into account the impact of colour perception defects, which affect a significant percentage of the population;

- rules on how information for patients is divided among the package leaflet and the outer packaging (including the inside of the box) in the case of self-medication products and how the most important information is highlighted: which information should go on the box and for what purpose? *Prescrire* requests that readability testing for package leaflets be applied to all licensed drugs, as stipulated in Directive 2004/27/EC; that the results of these tests be made systematically publicly accessible. *Prescrire* proposes that the principle of readability testing be extended to all the information present on a drug's packaging: so in addition to the package leaflet, this would include the labelling of every item of packaging (box, immediate packaging, dosing device) and any information displayed on boxes that is specific to non-prescription drugs, and any pictorial information (pictograms, signs, symbols). *Prescrire* proposes that user tests be conducted to study the risks of confusing similar packaging from the same commercial range;

- rules on the safety features of non-prescription (OTC) drugs must be discussed. Is it necessary to have a tamperproof seal or should patients be able to read the package leaflet before buying the product? How should access to demonstration or training devices be organised?

- rules for analysing the packaging of self-medication products should be applied by all Member State drug regulatory agencies, and not just the EMA (24);

In view of the risks involved, *Prescrire* proposes that the EMA plans in the coming months to develop guidelines on the dosing devices supplied with drugs, referring to the recent FDA guidelines (18).

In summary, it is time the European Commission broadened the scope of the regulation of drug safety, particularly for self-medication products, by demanding the EMA rethink its responsibility for preventing errors connected with drug naming, labelling and packaging items.

The new European rules on pharmacovigilance allow patients to report adverse effects; this measure should bring to light packaging defects identified by patients in real-life healthcare situations, particularly in self-medication.

The self-medication sector is too often led by the promotional activities of pharmaceutical companies and neglected by the authorities. It is time to stop considering European patients as passive consumers and to ensure that everyone has access to quality healthcare.

Olivier Huyghe for *Prescrire*'s editorial team

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