Rebuilding regulation after the Mediator° disaster: drug regulatory agencies must tackle the issue of packaging

The Mediator° disaster led to a major shake-up within the French drug regulatory agency in 2011 (see Prescrire Int n° 126 page 110). But the issue of packaging was overlooked in the raft of regulatory measures taken in 2011.

Packaging, the poor relation in drug re-assessments. For example, when commonly used paediatric drugs such as antitussives were re-assessed in France, their packaging was not questioned, although for the most part, it is dangerous (see inset page 135). Similarly, when pholcodine was reclassified as a prescription-only drug, no improvements in the packaging were imposed (see inset Prescrire Int n° 126 page 108).

The decision to improve the labelling of oral forms of methotrexate® is a welcome move, but other aspects of the packaging of the drugs concerned remain unsafe. A better alternative to dangerous bulk bottles must be demanded, such as blister packs with a safety film and a device to help patients with limited dexterity remove tablets or capsules from the blister pockets.

As of 2011, quinine is unfortunately still marketed for cramps in France. Fewer patients will be exposed to its adverse effects now that it is no longer reimbursed by the French national health insurance system, but some patients will continue to be at risk (Prescrire n° 337). The patient leaflets for the products concerned still do not inform patients about adverse effects, the bottle for Okimus® still has no child-proof cap, and blister packs containing Hexaquine® are still not labelled “quinine® (e)”.

The reclassification of mequitazine as a prescription-only drug does not alter the fact that the bottle is still not equipped with a child-proof cap and that a dose-measuring spoon is less accurate than a suitable oral delivery syringe (Prescrire n° 337).

Restricting the prescription of clonazepam - Rivotril® does not alter the fact that the bottle has no child-proof cap, that a dropper is a less efficient dosing device than a suitable oral delivery syringe. In addition, the blister pack and patient leaflet for these tablets are difficult to read (Prescrire n° 337).

Umbrella brands: evidence of the authorities’ lax attitude towards packaging. The current state of the pharmaceutical market gives the impression that the French and European regulatory agencies are too often following the lead of drug companies on the issue of packaging quality, especially concerning “umbrella” brands in the self-medication sector. In 2011, a ban on umbrella brands was still not forthcoming, and the problem continued to worsen with the authorisation of an oxomemazine product in a bottle with no child-proof cap, a dosing device (cup) liable to cause overdose, and unnecessarily fanciful labelling (Prescrire n° 337).

Differences between originator drugs and generics: a matter for regulators. Differences in dose strengths, concentrations and product packaging between originator drugs and generic versions are a potential source of medication errors. For example, a change in the formulation of originator drugs containing perindopril led to a difference in the expression of dose strength from that of the generic versions, creating a risk of overdose (Prescrire n° 316 and n° 327). Risks are likely now that the dosage form and concentration of docetaxel - Taxotere® (Prescrire n° 327) differ from generic versions. In 2011, a generic drug containing lidocaine + adrenaline was considered conducive to error because the concentration of adrenaline differed from that of the originator drug (1).

Drug regulatory agencies have a responsibility to focus first and foremost on patient safety in their decision-making and should anticipate practical differences between originator drugs and generics.

An initial reaction from the French agency in 2011. During the past year, Prescrire received a letter from the French agency responding to our 2010 packaging review (2). According to this letter, the agency is examining the cases presented in the review.

Furthermore, the French agency’s project to re-assess marketing authorisations granted before 2005 will hopefully lead to the withdrawal of drugs with a negative harm-benefit balance, thus avoiding the need to modify their dangerous packaging. For drugs that are kept on the market, the project should place greater emphasis on packaging (3).

Analysing successes and failures. More generally, drug regulatory agencies should make a careful study of the pharmaceutical sector, specifically focusing on the issue of packaging, in order to identify successes as well as failures. They would then be able to guide pharmaceutical companies with full knowledge of the facts, so that they all develop safe, appropriate packaging, focusing first and foremost on the interests of the various types of patients who use their drugs.

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Selected references from Prescrire’s literature search
- 1- Afssaps “Différence de concentration en adrénaline entre la Lidocaïne Aguettant Adrénaline et Xylocaïne Adrénaline” avril 2011: 1 page.