# 2020 Prescrire Packaging Awards

When *Prescrire* evaluates a drug's harm-benefit balance, the quality of the drug's packaging is one of the factors examined. Does the packaging ensure the safety of patients, their family and their carers, enabling the drug to be accurately and easily used? Conversely, are any aspects of the packaging dangerous, or does it lack anything necessary for the safe use of the drug?

Our packaging examinations take many factors into account: the clinical situation in which the drug will be used; the patients liable to receive it, especially pregnant women, children or elderly patients; whether family members, carers or a nurse will prepare and administer it; and whether it will be used in an emergency, hospital or community setting, obtained on prescription, on the advice of a community pharmacist, or bought by the patient from an internet retailer.

Every aspect of the packaging is assessed for quality and user safety. We examine in particular: whether international nonproprietary names (INNs) are clearly legible and whether different dose strengths of the same drug are easily distinguishable; the clarity of any information presented graphically, such as diagrams, dosing schedules, symbols or pictograms; the devices for preparing, measuring and administering doses; the risk that children will be able to ingest the drug unnoticed by their carers; and the quality and clarity of the information provided in the patient leaflet on how to use the product, its adverse effects, and the situations and patient groups in which the drug poses a particular risk.

The 2020 Prescrire Packaging Awards pertain to the packaging of drugs evaluated in our French edition in 2020.

## 2020 PACKAGING AWARDS

**Maviret°** tablets (***glecaprevir*** + ***pibrentasvir***) AbbVie (Rev Prescrire n° 439)
For the quality of its primary packaging, consisting of blister packs, each containing the daily dose of 3 tablets, and each blister pocket labelled with the INNs of both antiviral agents and their strengths. Also for its secondary packaging, which includes 4 boxes, each containing one week of treatment (7 blister packs with 3 tablets each), and a reminder of the dosing instructions on the lid of each box, stating "*take all 3 tablets in 1 blister once daily with food*" alongside a photo of the 3 tablets. This reminder helps patients take their treatment properly, enhancing the quality of packaging that also features boxes and blister packs that clearly identify the drugs they contain and their strength.

**Tiapridal°** oral solution (***tiapride***) Sanofi Aventis (Rev Prescrire n° 442)
For the improvements made to its packaging: addition of a child-proof cap and an oral dosing syringe graduated in milligrams of the drug, and labelled with its INN and the concentration of the solution. Previously, Tiapridal° had a dropper inserted into the neck of the vial that carried a risk of error when counting the number of drops, especially for high doses. A syringe graduated in milligrams of *tiapride* eliminates the need to convert the number of milligrams prescribed into the number of millilitres of product to be administered, which can lead to errors.

## RED CARDS

### Cytotoxic drugs packaged in bulk bottles

**Imeth°** 10 mg tablets (***methotrexate***) Nordic Pharma and **Méthotrexate Bellon°** tablets (***methotrexate***) Sanofi Aventis (**a**) (Prescrire Int n° 216); **Rubraca°** tablets (***rucaparib***) Clovis Oncology (Rev Prescrire n° 443); and **Talzenna°** hard capsules (***talazoparib***) Pfizer (Rev Prescrire n° 440)
When tablets or capsules supplied in bulk bottles are placed in a pill organiser, they are no longer identifiable, unlike dry oral forms packaged in perforated unit-dose blisters.

*Methotrexate*, *rucaparib* and *talazoparib* are cytotoxic drugs. With bulk bottles, there is a risk of accidentally spilling the contents and therefore a risk that someone other than the patient, especially a child, might ingest the drug. Even a child-proof cap does not prevent this potentially fatal risk.

### Switch from blister packs to bulk bottles: a decline in quality

**Lamictal°** 5 mg dispersible or chewable tablets (***lamotrigine***) GlaxoSmithKline (Rev Prescrire n° 445)
For switching from non-unit-dose blister packs to a bulk bottle. The child-proof cap is insufficient to eliminate all the harms associated with bulk bottles, such as accidental spillage of tablets and the risk that someone other than the patient, especially a child, might take them by mistake. A better option would have been to upgrade to perforated unit-dose blister packs, to ensure that tablets remain easily identifiable, and to add a child-resistant film.

### Packaging that increases the risk of dosing errors

**Haldol°** oral solution (***haloperidol***) Janssen (Rev Prescrire n° 441)
For persisting in marketing this drug in a dropper bottle unsuited to measuring doses greater than 2 mg (20 drops) due to the risk of miscounting the number of drops required (up to 100 drops in some cases). Up until early 2020, a *haloperidol* oral solution was marketed in a 100-ml bottle with an oral dosing syringe graduated in milligrams, well-suited to measuring doses greater than 2 mg. The disappearance from the market of the product supplied with a syringe, leaving only the one supplied in a dropper bottle, is a decline in quality, placing patients at greater risk than they were before.

***a-*** *The pharmaceutical company has informed us that Méthotrexate Bellon° is no longer marketed in France since late December 2020.*

**Istendo°** solution for endotracheopulmonary instillation (***acetylcysteine***) Delbert (Rev Prescrire n° 442)
For supplying this drug in 5-ml ampoules when the recommended doses are from 1 ml to 2 ml, for not providing a device with which to measure the volume to be administered, and for the scant explanation in the patient leaflet on how to prepare the dose to be administered.

**Preminor°** hard capsules (***ramipril*** + ***amlodipine***) Leurquin Mediolanum (Rev Prescrire n° 442) and **Triplixam°** tablets (***perindopril*** + ***indapamide*** + ***amlodipine***) Servier (Rev Prescrire n° 444)
For the strong resemblance between the boxes and primary packaging (bottle labels, blister pack films) of the various dose strengths of these fixed-dose combinations, and the consequent risk of wrong-dose errors.

Furthermore, Triplixam° is supplied in a bulk bottle with no child-proof cap, a container of very poor quality. The flow restrictor moderately reduces the risk of accidental spillage and the consequent risk that someone other than the patient, especially a child, might ingest the drug. However, the tablets are no longer identifiable when removed from the bulk bottle and placed in a pill organiser.

**Prexate°** solution for injection in a pre-filled syringe (***methotrexate***) Alfasigma (Rev Prescrire n° 438)
For failing to add a reminder on the box that the drug is for weekly administration, exposing patients to the risk of potentially fatal dosing frequency errors. In late 2019, the European Commission ratified measures recommended by the Pharmacovigilance Risk Assessment Committee (PRAC) aimed at preventing errors involving *methotrexate*, which included adding a reminder that injectable *methotrexate* products used for immunosuppression are administered once weekly.

## Insufficient efforts to prevent ingestion by children

**Buprénorphine/Naloxone Arrow°** Arrow Génériques and **Buprénorphine/Naloxone Mylan°** Mylan sublingual tablets (***buprenorphine*** + ***naloxone***) (Rev Prescrire n° 435)
For packaging these sublingual tablets in blister packs without a child-resistant film, in contrast to the originator Suboxone°, thereby exposing children to the risk of accidental ingestion of *buprenorphine* and *naloxone*, both of which have serious adverse effects. It is regrettable that the packaging of the generic versions of this fixed-dose combination is less safe than that of the originator.

**Bonasol°** oral solution (***alendronic acid***) X.O; the ***chlorhexidine*** 0.12% mouthwashes **Chlorhexidine Arrow°** Arrow Génériques, **Chlorhexidine Biogaran°** Biogaran, **Chlorhexidine Mylan°** Mylan, **Paroex°** Centre Spécialités Pharmaceutiques, and **Prexidine°** X.O; the ***chlorhexidine*** 0.20% mouthwash **Eludrilperio°** Pierre Fabre Médicament; **Fluisédal°** syrup (***promethazine*** + ***meglumine benzoate*** + ***polysorbate 20***) Elerté; and **Tussisédal°** syrup (***promethazine*** + ***noscapine***) Elerté (Rev Prescrire n° 438)

For the absence of a child-proof cap on the bottles of these 9 products. Children are insufficiently protected by an ordinary cap, which gives them easy access to the contents of these bottles and puts them at risk of exposure to the adverse effects of the drugs they contain.

Boxes and bottles of Bonasol° lack a prominent reminder that it is for weekly administration, increasing the risk of dosing errors.

Fluisédal° and Tussisédal° have several dangerous packaging flaws: insufficient prominence is given to INNs and dose strengths on the boxes and bottles, the dosing device provided (a measuring spoon) is inaccurate, and the box lacks a pictogram indicating the risks posed during pregnancy, due in particular to the presence of *promethazine*.

## Patient leaflets that understate the product's harms

**Prontadol°** tablets (***paracetamol*** + ***caffeine***) Ipsen (Rev Prescrire n° 442)
For failing to adequately inform users of the hepatic harms associated with *paracetamol* overdose. Despite the statement on the box "*overdose = danger*", the patient leaflet does not explain the nature of the danger or describe the signs suggestive of *paracetamol* poisoning.

**Flector°** non-gastro-resistant tablets (***diclofenac***) Genévrier (Rev Prescrire n° 438) and **Nurofenplast°** medicated plasters (***ibuprofen***) Reckitt Benckiser (Rev Prescrire n° 435)
For providing insufficient information in the patient leaflet about the dangers of exposure to nonsteroidal anti-inflammatory drugs (NSAIDs) during pregnancy. The patient leaflet for Flector° does not rule out its use during the first 5 months of pregnancy, since the warning in the pregnancy pictogram only states: *"Not to be used by pregnant women from the 6$^{th}$ month of pregnancy"*.

The patient leaflet for Nurofenplast° does not warn patients about the risks of using these medicated plasters during the first 6 months of pregnancy, despite the pictogram on the box rightly prohibiting its use throughout pregnancy.

NSAIDs should be avoided throughout pregnancy, because there is no evidence that a contraindication starting at the sixth month of pregnancy is sufficient to eliminate the risk of harming the unborn child. Taking an NSAID during the first days of pregnancy can provoke spontaneous abortion.

Furthermore, insufficient prominence is given to the INNs of these 2 NSAIDs on the packaging of these products, making it difficult for patients to identify their composition, and increasing the risk that they might be used by women who are or could become pregnant.