Noteworthy: sodium bicarbonate tablets with marketing authorisation, an old drug that is useful in metabolic acidosis associated with chronic kidney disease. Patients with chronic kidney disease can develop metabolic acidosis with potentially serious clinical consequences. *Sodium bicarbonate* is a drug of choice, with probable efficacy in limiting the progression of renal failure, and possibly in reducing mortality.

It is an old drug, of course. The new development honoured in the 2024 Prescrire Drug Awards is that *sodium bicarbonate* gastro-resistant tablets have been granted marketing authorisation in France, where, previously, oral *sodium bicarbonate* was only available as an extemporaneous preparation. This marketing authorisation constitutes a therapeutic advance because it guarantees high-quality manufacturing standards and labelling, including the provision of a patient leaflet.

Bicafres° earned the title of Noteworthy drug in recognition of this administrative procedure, which guarantees the quality of a cheap and useful drug.

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2024 Prescrire Packaging Awards

When Prescrire evaluates a drug's harm-benefit balance and ease of use, its packaging is an important factor to take into account and analyse. Does the packaging help ensure the safety of patients, their families and their caregivers? Do any aspects of the packaging increase the risk of medication errors or pose a particular danger? Is the packaging well-designed from the users' perspective, enabling accurate measurement of the doses to be administered, for example?

Our packaging analyses take many factors into account, including: the clinical situations in which the drug will be used; the patients liable to receive it, such as pregnant women, children, or older adults or patients with a disability who may, for example, have reduced manual dexterity; whether family members, carers or nurses will prepare and administer the drug; the context in which it will be used (e.g. in a healthcare facility, possibly in an emergency setting); and whether it will be obtained on prescription or on the advice of a community pharmacist.

Every aspect of the packaging is analysed for its impact on quality of care and the safety of patients and the people around them. 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 showing how to prepare the dose to be administered, dosing schedules, symbols or pictograms;
– The devices provided for dose preparation, measurement or administration;
– The quality, intelligibility and clarity of the information provided in the patient leaflet, especially in the sections on how to use the product, its adverse effects, and the situations and patient populations in which the drug poses a particular risk;
– The risk of accidental ingestion, for example by a child.

The 2024 Prescrire Packaging Awards pertain to the packaging of drugs evaluated in our French edition in 2024. One product has earned an award for its particularly well-designed packaging. Those for which we identified packaging flaws that increase the risk of medication errors or pose other dangers received a Packaging Red Card.

One Packaging Award in 2024

A product with well-designed packaging, marketed in France

Lidocaine Aguettant 10 mg/ml solution for injection in pre-filled syringes (***lidocaine***) - Aguettant (*Rev Prescrire* n° 494)

Pre-filled syringes containing 100 mg of *lidocaine* in 10 ml of solution per syringe (10 mg/ml) are authorised in France for local anaesthesia and peripheral nerve block in adults and children from 2 years of age, and for intravenous regional anaesthesia of the upper limbs in adults. Prescrire examined this product when it became available in the community, rather than just in hospitals. This ready-to-use presentation simplifies aseptic preparation of the injection. It is both convenient for healthcare professionals and safe for patients.

Packaging Red Cards

11 dry oral forms packaged in multidose bottles, authorised in the European Union

Ayvakyt° tablets (***avapritinib***) - Blueprint Medicines (*Prescrire Int* n° 262)
Biktarvy° tablets (***bictegravir*** 30 mg + ***emtricitabine*** 120 mg + ***tenofovir alafenamide*** 15 mg) - Gilead Sciences (*Prescrire Int* n° 261)
Brukinsa° hard capsules (***zanubrutinib***) - Beigene (*Prescrire Int* n° 261)
Cufence° hard capsules (***trientine***) - Intsel Chimos (*Rev Prescrire* n° 493)
Genvoya° tablets (***elvitegravir*** 90 mg + ***cobicistat*** 90 mg + ***emtricitabine*** 120 mg + ***tenofovir alafenamide*** 6 mg) - Gilead Sciences (*Prescrire Int* n° 265)

Opfolda° hard capsules (***miglustat***) - Amicus Therapeutics (*Prescrire Int* n° 267)
Orgovyx° tablets (***relugolix***) - Accord Healthcare (*Prescrire Int* n° 264)
Tibsovo° tablets (***ivosidenib***) - Servier (*Rev Prescrire* n° 265)
Triumeq° tablets (***dolutegravir*** 5 mg + ***abacavir*** 60 mg + ***lamivudine*** 30 mg) - ViiV Healthcare (*Rev Prescrire* n° 485)
Wakix° tablets (***pitolisant***) - Bioprojet Pharma (*Prescrire Int* n° 260)
Zokinvy° hard capsules (***lonafarnib***) - Intsel Chimos (*Prescrire Int* n° 262)

Multidose bottles have several disadvantages compared with pre-cut unit-dose blister packs. For example, when the tablet or capsule is removed from the bottle and placed in a pill organiser, at home or in a healthcare or residential care facility, it is more difficult to identify the drug and its dose strength, and the drug is less well protected from environmental conditions such as humidity or light. There is also a greater risk of accidental spillage of the bottle's contents and, consequently, of accidental ingestion of the drug by someone other than the patient, especially a child.

4 products authorised in France with labelling that fails to inform patients and healthcare professionals about certain risks

Cabesol° shampoo - Medgen, **Clobetasol Substipharm°** shampoo - Substipharm, **Clobex°** shampoo - Galderma (***clobetasol***) (*Rev Prescrire* n° 490)
Mantadix° capsules (***amantadine***) - X.O (*Rev Prescrire* n° 493)

6 products with packaging flaws that increase the risk of administration errors, including 3 European authorisations

Vivotif° capsules (***Salmonella enterica serovar Typhi***) - Imaxio (*Rev Prescrire* n° 492) (French authorisation)

Pentacarinat° powder for aerosol and for parenteral use - Sanofi Winthrop, **Pentamidine Tillomed°** powder for solution for injection or nebulisation - Tillomed Pharma (***pentamidine***) (*Rev Prescrire* n° 489) (French authorisations)

Vabysmo° solution for intravitreal injection (***faricimab***) - Roche (*Prescrire Int* n° 260)

As with other solutions for intravitreal injection that contain a VEGF inhibitor, such as *aflibercept* (Eylea° or other brands) and *ranibizumab* (Lucentis° or other brands), the volume of *faricimab* solution to be injected into the eye is only a fraction of the contents of the vial. However, the entire contents of the vial must be withdrawn using a filter needle supplied in the box. A new needle is then attached to the syringe, and the surplus solution in the syringe must be expelled before performing the intravitreal injection. In contrast to the vials or pre-filled syringes of other VEGF inhibitors for intravitreal use, the need to expel the surplus volume before giving the injection is not stated on the box of Vabysmo°. The absence of this warning exposes patients to a risk of overdose and increased intraocular pressure.

Fintepla° oral solution (***fenfluramine***) - UCB Pharma (*Prescrire Int* n° 263)

The amphetamine *fenfluramine* (Fintepla°) is authorised as a 2.2 mg/ml oral solution for use in children with certain severe forms of epilepsy. It is administered using an oral syringe graduated in millilitres. The box of Fintepla° contains 2 green 3-ml syringes with 0.1-ml graduations from 0 ml to 3 ml, and 2 purple 6-ml syringes with 0.2-ml graduations between 3 ml and 6 ml. The doses are expressed in mg/kg/day in the SmPC for Fintepla°. The SmPC does not include a conversion table showing the volume in millilitres to administer at each of the twice-daily doses. It simply gives two examples of conversions in the dosage tables, corresponding to the maximum recommended doses, e.g. "*13 mg twice daily i.e. 6.0 ml twice daily*". The patient leaflet is no more explicit on this point, simply stating "*You will be told how many ml to take for each dose*". A further risk of wrong-dose errors is created by the presence of 2 syringes of different capacities.

Tepkinly° solution for injection (***epcoritamab***) - AbbVie (*Prescrire Int* n° 268)

Epcoritamab (Tepkinly°), authorised in certain diffuse B-cell lymphomas, is supplied as a concentrate for solution for injection (dose strength 4 mg/0.8 ml) or as a ready-to-use solution for injection (dose strength 48 mg/0.8 ml). The 4 mg/0.8 ml concentrate is used to prepare the first 2 weekly injections. The 48 mg/0.8 ml solution is used for subsequent injections. The concentrate is diluted twice for the first dose and once for the second dose. 1 or 2 empty vials are required for the dilution steps, which are not supplied in the box of Tepkinly°. This product has several features that increase the risk of wrong-dose errors: the unusual preparation method, the need to dilute the solution once or twice for some doses but not for others, resemblance between the 2 dose strengths expressed on the boxes, and the fact that the volume of solution present is not stated on the box of the 48-mg dose strength.

Miscellaneous: an unsuitable dosing device; insufficiently addressed preparation and handling errors; and a paediatric indication for which no usable presentation is available

Amisulpride Stragen° oral solution (***amisulpride***) - Stragen (*Rev Prescrire* n° 486) (French authorisation)
Eligard° powder and solvent for solution for injection (***leuprorelin***) - Bouchara-Recordati (*Rev Prescrire* n° 490) (French authorisation)
Fragmine° 2500 IU (of anti-factor Xa activity)/0.2 ml solution for injection in pre-filled syringes (***dalteparin***) - Pfizer (*Rev Prescrire* n° 487) (French authorisation)

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