# THE PRESCRIRE AWARDS FOR 2023

The annual Prescrire Awards are granted in total independence by the Prescrire Editorial Staff.

## 2023 Prescrire Drug Awards

Every month, Prescrire's Editorial Staff help health professionals decide which of the multitude of newly authorised products or indications are worth adding to their list of useful treatment options, and which are to be avoided. We do this by conducting systematic analyses of the relevant evaluation data available on new drugs, new indications, new pharmaceutical forms and new dose strengths authorised in Europe or in France. European authorisations account for the majority, and these are the focus of our English edition, *Prescrire International*. The 2023 Prescrire Drug Awards are based on the reviews published in the Marketing Authorisations section of our French edition in 2023.

Prescrire's multidisciplinary team has been conducting and publishing independent drug analyses for 43 years, free from the influence of any companies involved in the healthcare sector.

### No Pilule d'Or, and only one Prescrire Drug Award

None of the drugs examined by Prescrire in 2023 represented a major therapeutic advance worthy of a Pilule d'Or (Golden Pill Award). Only one drug received an award, earning a place on the Honours List.

**Honours List: blinatumomab (Blincyto®) in high-risk first-relapse acute lymphoblastic leukaemia in children.** Acute lymphoblastic leukaemia (ALL) relapses in about 15% to 20% of children following first-line treatment. The relapse is considered high-risk when it occurs within 18 months of diagnosis or within 6 months of completing first-line treatment. It is usually treated with several phases of chemotherapy, with no standard protocol.

The anti-CD19 and anti-CD3 bispecific monoclonal antibody *blinatumomab* was evaluated as consolidation therapy in children with Philadelphia chromosome-negative high-risk first-relapse ALL in a non-blinded randomised trial versus chemotherapy in 108 patients. When half of the patients had been followed up for at least 31 months, mortality in the *blinatumomab* group was about 17%, versus 43% in the chemotherapy group. Some longer-term data have been published since we last searched the literature for our initial article about this authorisation (1). According to these data, obtained when half of the patients had been followed up for at least 44 months, the estimated 4-year mortality was 23% in the *blinatumomab* group, versus 51% in the control group. These differences in mortality are statistically significant.

Another non-blinded randomised trial compared *blinatumomab* to chemotherapy, using a different dosage of *blinatumomab* from that recommended in the European summary of product characteristics (SmPC). The results also showed lower mortality in the *blinatumomab* group.

The main adverse effects of *blinatumomab* are: neurological disorders, pancreatitis, tumour lysis syndrome and haematological disorders. In these trials, *blinatumomab*'s serious adverse effects appeared to be less frequent than those of the chemotherapy received in the control groups. However, the quality of this evidence is weakened by the absence of blinding.

A notable reduction in mortality, demonstrated in two randomised comparative trials in children with high-risk first-relapse ALL, is a clear therapeutic advance that justifies *blinatumomab*'s place on this year's Honours List.

*Blinatumomab* illustrates how a drug's harm-benefit balance depends on the clinical situation. In the absence of evidence that *blinatumomab* improves clinical outcomes in adults with ALL who are in remission but have residual leukaemic cells, its harm-benefit balance in that situation is unfavourable (see *Prescrire Int* n° 223).



► Translated from *Rev Prescrire* February 2024
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**1-** Locatelli F et al. "Improved survival and MRD remission with blinatumomab vs. chemotherapy in children with first high-risk relapse B-ALL" *Leukemia* 2023; **37** (1): 222-225.

**Pilule d'Or/Golden Pill**

A Pilule d'Or (Golden Pill) is awarded to drugs that represent a major therapeutic advance in a particularly poorly served field.

**Not awarded in 2023**

**2023 Honours List**

Drugs included on the Honours List constitute a clear advance for some patients compared with existing therapeutic options, albeit with limitations.

**Blincyto® (*blinatumomab*) Amgen**

In high-risk first-relapse acute lymphoblastic leukaemia in children (*Prescrire Int* n° 248)

**Noteworthy**

Drugs deemed "Noteworthy" provide a modest improvement in patient care.

**No Noteworthy drugs in 2023**

# 2023 Prescrire Packaging Awards

When Prescrire evaluates a drug's harm-benefit balance or its ease of use, its packaging is an important factor to take into consideration. 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, and in particular can the doses required be measured accurately?

Our packaging analyses 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 older people; whether family members, carers or nurses will prepare and administer the drug; and whether it will be used in an emergency setting, in hospitals or in the community, 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 analysed for its impact on quality of care and the safety of users 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, dosing schedules, symbols or pictograms;
– The devices provided for preparing, measuring and administering doses;
– The risk that someone other than the patient, especially children, could ingest the drug, unnoticed by their carers;
– The quality and clarity of the information provided in the patient leaflet, especially information on how to use the product, its adverse effects, and the situations and patient groups in which the drug poses a particular risk, as well as any information made available through a QR code on the box.

The 2023 Prescrire Packaging Awards pertain to the packaging of drugs evaluated in our French edition in 2023. Two products have earned an award for their particularly well-designed packaging. However, various products received a "Red Card" because their packaging is liable to cause medication errors or poses other dangers.

## 2023 Prescrire Packaging Awards

### Packaging well-designed for the oral administration of high doses of dexamethasone

**Dexliq°** oral solution (***dexamethasone***) - Theravia (French authorisation) (*Rev Prescrire* n° 473)

### Packaging that made intranasal fentanyl safer to use

**Instanyl°** DoseGuard° nasal spray solution (***fentanyl***) - Takeda (EU centralised procedure) (*Prescrire Int* n° 257)

Intranasal *fentanyl* is authorised for the relief of breakthrough pain in cancer patients, as an add-on to well-conducted maintenance opioid therapy. *Fentanyl* nasal spray was initially marketed under the brand name Instanyl° in a multidose spray bottle enclosed in a child-resistant box, with no lock-out mechanism to prevent overdoses. Single-dose spray containers, in secondary packaging protected by a child-resistant film, were subsequently marketed alongside these multidose bottles but, in France at least, they were only available in hospitals.

*Fentanyl* nasal spray was marketed in new packaging in 2023, under the brand name Instanyl° DoseGuard°, consisting of a multidose spray bottle with a child-proof cap and a button on the side to unlock the device. An electronic dose management system limits the number of successive doses to 2, in accordance with the recommendation in the SmPC to treat each episode of breakthrough pain with no more than 2 doses, administered at least 10 minutes apart.

In practice, when 2 successive doses are administered within a 60-minute period, an automatic lock-out mechanism prevents any further administrations for 2 hours. This system is designed to limit accidental overdoses, which can be fatal. The priming procedure is complex, and patients must learn how the lock-out system works, but Instanyl° DoseGuard° succeeds in making opioid use safer for patients and the people around them, especially children, while at the same time allowing some flexibility in adjusting the dose to the level of pain experienced by patients, both in the community and in hospitals.

## Red Cards

### 39 drugs authorised in the European Union or France in poor-quality packaging received a "Red Card" for various reasons:

– Dry oral forms supplied in multidose bottles: difficult to identify the drug once removed from the bottle, and risk of accidental drug exposure, especially in children;
– Oral liquid forms supplied in bottles with no child-proof cap: risk of accidental drug exposure, especially in children;
– An oral solution supplied in a dropper container, with a recommended dose of up to 60 drops: risk of wrong-dose errors;
– Look-alike packaging: risk of wrong-drug errors;
– Insufficient prominence given to INNs: difficult to identify the drug substance(s) present;
– Incomplete information concerning risks during pregnancy: risk of embryotoxicity, fetotoxicity or pregnancy complications.



► Excerpt from *Rev Prescrire* February 2024
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# 2023 Prescrire Information Awards

Prescrire's annual Information Awards are based on the quality of the documentation and information provided by pharmaceutical companies in response to requests by Prescrire's Editorial Staff. We use this documentation when preparing the articles published in the Marketing Authorisations section of our French edition. Prescrire's Information Awards focus on the level of transparency that companies have exhibited over the year in response to our requests for information and documentation.

**What information does Prescrire request from pharmaceutical companies, and why?** In addition to the information Prescrire gathers through a systematic search of the scientific literature and documentation provided by health authorities, we systematically ask pharmaceutical companies to send us data on their drugs, from marketing authorisation through to post-marketing surveillance.

We primarily ask for data on efficacy and adverse effects, packaging items, the conditions under which patients can access the drug, its reimbursement status in France, the planned date of its market introduction or the reasons for its market withdrawal.

We request all of this information in order to provide healthcare professionals with updated scientific knowledge with which to evaluate the harm-benefit balance of the drug in question, promote the correct use of drugs and help ensure patient safety, and also to share practical information about availability, reimbursement and so on.

**Transparency very often limited.** Prescrire requested information from 89 pharmaceutical companies in 2023.

Six of them earned a place on the 2023 Information Awards Honours List, by responding with detailed documentation that addressed every aspect of Prescrire's requests. Four of them were rated as "Outstanding" for sending particularly useful information and documents in a timely manner: Amryt Pharmaceuticals, EG Labo, Ever Pharma, and Theravia (formerly Cell Therapies Research & Services).

The pharmaceutical companies on the 2023 Information Awards Honours List chose to be open, and demonstrated that transparency is feasible, by providing documents or information that are not publicly available, such as:

– Clinical study reports (CSRs), which contain details on the protocols and results of clinical trials, especially on adverse effects;
– Periodic safety update reports (PSURs), which enable a better understanding of the drug's adverse effects;
– Documentation submitted to the French National Authority for Health (HAS) to request eligibility for reimbursement by the national health insurance system or approval for use in hospitals. These documents contain useful clinical and administrative data;
– Information about when their monopoly will end, and when generic versions of the drug can be marketed;
– Information about the date the drug will enter the market;
– Packaging items.

Conversely, 13 pharmaceutical companies chose to withhold information from Prescrire. They failed to respond to repeated requests, some claiming that they do not have time, while others clearly indicated their choice not to provide information to Prescrire. These companies received an information "Red Card" (see figure).

**Transparency: not just a principle, but a duty for drug companies.** Pharmaceutical companies hold a wealth of documents that they usually make inaccessible to the public, in particular certain evaluation data. European citizens have the right to access clinical data on which marketing authorisations are based. Evaluation data are not confidential data. In fact, the European Ombudsman considered the argument that disclosure of clinical study reports could undermine companies' commercial interests to be unfounded. The European Medicines Agency (EMA) itself deemed as "releasable" documents containing clinical data received in connection with European evaluations, such as PSURs and CSRs. And when the EMA was challenged by pharmaceutical companies for having divulged these data, the European Court of Justice ruled in the EMA's favour. Pharmaceutical companies have a duty to provide medical information, and this includes a responsibility to share clinical data.

**It is possible to provide high-quality information, but it remains the exception.** In 2023, some pharmaceutical companies showed that a commitment to openness and a company policy of transparency are possible. They serve as examples for all the others to follow.



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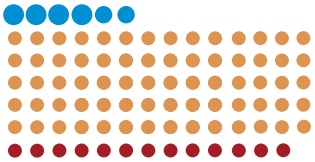
## Prescrire Information Awards

**Of the 89 companies we contacted for information**



- **6 companies made the Honours List**
- **70 companies not on the Honours List not given a Red Card**
- **13 companies given a Red Card**

**Honours List**

**Outstanding:**
**Amryt Pharmaceuticals, EG Labo, Ever Pharma, Theravia (formerly Cell Therapies Research & Services)**

**Followed by:**
Arrow Génériques, Lundbeck

**Red Cards**

Alk-Abelló, Amgen, Bayer Healthcare, Bristol-Myers Squibb, Genzyme (Sanofi Group), Incyte Biosciences, Janssen Cilag, Kyowa Kirin Pharma, Menarini, MSD, Sanofi Aventis (Sanofi Group), Vifor Fresenius Medical Care Renal Pharma, X.O.