THE PRESCRIRE AWARDS FOR 2017

The three annual Prescrire Awards, for Drugs, Packaging and Information, are granted in total independence by the Prescrire Editorial Staff. The rules governing the three Prescrire Awards are available online at english.prescrire.org.

2017 Prescrire Drug Awards

New products or new indications eligible for the Prescrire Drug Awards are those evaluated during the previous year in the New Products section of our French edition.

Each month, the *Prescrire* Editorial Staff publish systematic analyses of the data available on: new drugs, new indications authorised for existing drugs, and existing drugs marketed in a new form or with different packaging. The goal is to help readers distinguish, among the plethora of new products, those worth adding to their list of useful therapies, those worth using instead of older products, and those to be avoided.

Our analyses are based on rigorous procedures, described in detail at english.prescrire.org. The *Prescrire* Editorial Staff conduct these analyses free from any industry or institutional influence. Our independence is made possible by the fact that we are financed exclusively by our subscribers, carry no paid advertising in either the French or the English edition, and receive no grants or subsidies of any kind.

The *Prescrire* Drug Awards are compiled at the end of each year, based on the reviews published that year in our French edition, and taking into account any new data made available since the initial articles were published. These awards honour drugs that constitute a therapeutic advance, in that they offer better efficacy, less frequent or less severe adverse effects (for similar efficacy), or safer or easier administration.

Three drugs received a Prescrire Award for 2017. Three drugs received a Prescrire Drug Award this year: one that earned a place on the Honours List, and two that were deemed "Noteworthy" (see overleaf).

Asfotase alfa (Strensiq°) in perinatal and infantile hypophosphatasia. Hypophosphatasia is a rare inherited disease caused by an enzyme deficiency. Perinatal forms have a mortality approaching 100%, while over 50% of babies who develop signs and symptoms before the age of 6 months (infantile forms) die in the first year of life.

Asfotase alfa is a recombinant protein that reproduces the activity of the deficient enzyme. The results of two non-comparative clinical trials in a

"PILULE D'OR" NOT AWARDED FOR 2017

Pilule d'Or / Golden Pill

The Pilule d'Or (Golden Pill) is granted to drugs that constitute a major therapeutic advance in a field in which no treatment was previously available.

2017	NOT AWARDED
2014 (Prescrire Int n° 157)	ORPHACOL° (*cholic acid*)
2007 (Prescrire Int n° 94)	CARBAGLU° (*carglumic acid*) (a second look)
2006 (Prescrire Int n° 88)	ORFADIN° (*nitisinone*)
1998 (Prescrire Int n° 40)	CRIXIVAN° (*indinavir*)
1996 (Prescrire Int n° 28)	DIGIDOT° (*digoxin-specific antibody*) (**a**)
1992 (Prescrire Int n° 4)	SURFEXO° (*pulmonary surfactant*) (**a**)
1989 (Rev Prescrire n° 92)	EPREX° (*epoetin alfa*) • MECTIZAN° (*ivermectin*)
1988 (Rev Prescrire n° 81)	LARIAM° (*mefloquine*) • RETROVIR° (*zidovudine*)
1987 (Rev Prescrire n° 71)	LUTRELEF° (*gonadorelin*) • DÉCAPEPTYL° (*triptorelin*)
1986 (Rev Prescrire n° 61)	ZOVIRAX° IV and tablets (*aciclovir*)
1983 (Rev Prescrire n° 31)	LOPRIL° (*captopril*)
1981 (Rev Prescrire n° 10)	VACCIN HEVAC B° (*hepatitis B vaccine*) (**a**)

No Golden Pill was awarded for 1982, 1984, 1985, 1990, 1991, 1993–1995, 1997, 1999–2005, 2008–2013, 2015, or 2016.

a- No longer marketed in France as of 2017.

Honours List

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

2017	• **STRENSIQ° (*asfotase alfa*) Alexion** Perinatal and infantile forms of hypophosphatasia (Prescrire Int n° 187)
2015 (Prescrire Int n° 162)	• Hemangiol° (*propranolol* oral solution)
2014 (Prescrire Int n° 157,154, 156)	• Glivec° (*imatinib*) • Malacef° (intravenous *artesunate*) • Sovaldi° (*sofosbuvir*)
2010 (Prescrire Int n° 114)	• Glivec° (*imatinib*)
2007 (Prescrire Int n° 98)	• Glivec° (*imatinib*) • Herceptin° (*trastuzumab*)
2006 (Prescrire Int n° 84)	• Egaten° (*triclabendazole*)
2005 (Prescrire Int n° 77)	• Varivax° (*varicella-zoster vaccine*)
2004 (Prescrire Int n° 76)	• Diacomit° (*stiripentol*) • Fuzeon° (*enfuvirtide*) • Morphine Aguettant° syrup (*morphine* oral solution) (**a**)
2003 (Prescrire Int n° 66,69,74)	• Carbaglu° (*carglumic acid*) • IVheBex° (*hepatitis B immunoglobulin*) • Meningitec° (*conjugate meningococcal C vaccine*)(**a**)

Drugs were included on the Honours List every year between 1981 and 2007. No drugs were included for 2008, 2009, 2011–2013, or 2016. The full list of drugs included on the Honours List from 1981 to 2013 can be found in *Prescrire Int* n° 147 p. 79.

a- No longer marketed in France as of 2017.

Noteworthy

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

2017	• **PERJETA° (*pertuzumab*) Roche** Metastatic breast cancer, in combination with trastuzumab and docetaxel in certain patients (Prescrire Int n° 184)
	• **TRUVADA° (*emtricitabine + tenofovir disoproxil*) Gilead Sciences** Prevention of HIV transmission in patients at high risk (Prescrire Int n° 187) (**a**)

a- Generic versions with better packaging than Truvada° were available in France in 2017 (see the Packaging Awards on p. 81).

total of 70 infants and children younger than 5 years old, all treated with *asfotase alfa*, suggest that this drug greatly reduces mortality and the bone disorders associated with this disease. None of the documents identified in our literature search give a breakdown of the results by age group, in particular for infants younger than 6 months old, who have the most serious forms of the disease. This is an important weakness in the drug's evaluation. In addition, the effects of *asfotase alfa* on the complications of the disease other than bone disorders are unknown. The main known adverse effects are injection site reactions, hypersensitivity reactions, and probably ectopic calcifications.

Pertuzumab (Perjeta°) in certain patients with metastatic breast cancer. In women with HER2-overexpressing metastatic breast cancer, longer-term results from a single clinical trial in 808 patients showed that adding the anti-HER2 antibody *pertuzumab* to the *trastuzumab* + *docetaxel* combination increases the proportion of women alive after 4 years by about 12 percentage points (54% versus 42%) and prolongs median survival by about 16 months. This benefit was observed in patients who for the most part had not previously received *trastuzumab* and exhibited no cardiac dysfunction before inclusion in the trial. It is for these women particularly that *pertuzumab* constitutes a therapeutic advance. *Pertuzumab*'s main adverse effects are potentially severe diarrhoea, febrile neutropenia, mucocutaneous disorders, infusion reactions, and heart failure.

Emtricitabine + tenofovir disoproxil (Truvada° or other brands) to prevent HIV transmission in patients at high risk. The main methods for preventing HIV transmission between serodiscordant partners who have penetrative sex are systematic condom use and antiretroviral treatment of the infected person. However, some people engage in sexual behaviour that carries a high risk of HIV transmission but do not use condoms.

Two clinical trials conducted in men who have anal sex with men have shown that pre-exposure prophylaxis with the antiretroviral combination *emtricitabine* + *tenofovir disoproxil*, taken every day or only during periods of sexual activity, considerably reduces (without eliminating) the risk of acquiring HIV infection, and has acceptable adverse effects. This type of prophylaxis can increase high-risk behaviour in those who mistakenly believe it affords complete protection and could increase the frequency of other sexually transmitted infections. It is also associated with a poorly documented risk of developing HIV infection that is resistant to the antiretrovirals used for prophylaxis.

In summary. The three drugs that received a Prescrire Drug Award for 2017 are indicated for very different diseases. Three awards for a total of 92 drug analyses published in 2017 is a very low success rate. And for the third year running, none of the drugs examined offered a therapeutic advance worthy of a Golden Pill/Pilule d'Or.

▶ Translated from *Rev Prescrire* **February 2018**
Volume 38 N° 412 • Pages 84-85

2017 Prescrire Packaging Awards

The Packaging Awards focus on the quality of the packaging of drugs evaluated in 2017 in our French edition.

2017 Packaging Award

• **Emtricitabine + tenofovir disoproxil Mylan°** tablets, Mylan (Prescrire Int n° 187)
Prominence is given on the box to the information that is useful in patient care and helps prevent medication errors, i.e. the international nonproprietary names (INNs) and dose strengths. The tablets are packaged in pre-cut unit-dose blister packs, where each detachable blister pocket is labelled with the INNs, dose strengths, batch number, and expiry date. Pre-cut unit-dose blister packs ensure that tablets remain identifiable, traceable and protected in many situations: in the home, or away from home; when a third party administers the drug; in hospitals that operate a unit-dose drug distribution system; etc. The *emtricitabine + tenofovir disoproxil* combination has been available in France since 2006 in bulk bottles containing 30 tablets, under the brand name Truvada°. Bulk bottles have several drawbacks: tablets can only be identified on the basis of their appearance, are unprotected once removed from the bottle, and must be repackaged in hospitals to enable unit-dose drug distribution.
Emtricitabine + tenofovir disoproxil Mylan° was marketed in 2017 and is the first unit-dose format of this combination to be made available in France.

Prescrire's systematic reviews include evaluation of the drug's packaging. Does the packaging make the drug easy and safe to use? Do any aspects of the packaging constitute a therapeutic advance? Conversely, are any aspects of the packaging dangerous?

When *Prescrire* analyses a drug's packaging, we consider the context in which the drug will be obtained, prepared and administered: the situations in which it will be used; the patients likely to receive it, especially if they are children, pregnant women or elderly patients; whether it will be used in an emergency, hospital or community setting, obtained on prescription, on the advice of a community pharmacist, or bought on the patient's own initiative from a pharmacy or an internet retailer; whether or not a nurse will prepare and administer it; etc.

Every aspect of the packaging is examined to determine its quality and safety. We examine: the legibility of international nonproprietary names (INNs), whether different dose strengths are easily distinguishable, and any information presented graphically, such as dosing schedules and pictograms; any dosing devices supplied to prepare and administer the required doses; the measures taken to protect children from poisoning; and the quality and clarity of the information provided in the patient leaflet on dose preparation, adverse effects, and the situations and patient groups in which the drug poses a risk.

The *Prescrire* Packaging Awards are based on independent evaluations conducted by *Prescrire*'s Editorial Staff and our Packaging Working Group, free from any influence from packaging manufacturers.

YELLOW CARDS

Vogalib° oral lyophilisate **(*metopimazine*)** Procter & Gamble Pharmaceuticals (Rev Prescrire n° 403)
For not giving due prominence on the box or blister packs to the INN, whereas every possible effort should be made to help patients and health professionals identify the presence of *metopimazine*, a drug with neuroleptic properties.

Bactérix° hard capsules **(*nifuroxazide*)** Gifrer Barbezat (Prescrire Int n° 187)
For not displaying the INN on the blister pack, which makes it difficult for patients and health professionals to identify the presence of *nifuroxazide*, a drug that can provoke severe allergic reactions and immunological adverse effects.

Skudexum° tablets **(*tramadol* 75 mg + *dexketoprofen* 25 mg)** Menarini (Rev Prescrire n° 409)
For giving insufficient prominence on the box and blister pack to the INNs and the quantity of *tramadol* present. The labelling therefore makes it difficult to understand the composition of the tablets, yet patients and health professionals ought to be able to easily identify the presence of opioids in medicines to avoid any confusion, and in particular the risk of unwitting concomitant use of several opioid-containing medicines.

RED CARDS

DANGEROUSLY LIMITED INFORMATION IN THE LABELLING OR PATIENT LEAFLET, INCLUDING UMBRELLA BRANDS

Drill Maux de Gorge° tablets and syrup (***alfa-amylase***), **MucoDrill°** effervescent tablets (***acetylcysteine***) Pierre Fabre Médicament (Rev Prescrire n° 399) • **Lysopaïne Maux de Gorge Ambroxol°** oromucosal spray, solution (***ambroxol***) Sanofi Aventis (Prescrire Int n° 184) **Humex Mal de Gorge°** lozenges (***lidocaine + dichlorobenzyl alcohol + amylmetacresol***) Urgo Healthcare (Rev Prescrire n° 399) • **Clarix état Grippal°** powder for oral solution in sachets (***paracetamol + chlorphenamine + vitamin C***) Coopération Pharmaceutique Française (Rev Prescrire n° 400)
The principle of an umbrella brand is to sell various medicines containing different active substances, with different dangers, under the same trademark. This marketing strategy, based on brand recognition, can lead to confusion between drugs of the same umbrella brand and unawareness of certain risks, such as drug interactions. The risk of error is increased by the visual resemblance between medicines, which all display the umbrella brand name in large, bold characters and share the same typographic style and graphics. INNs are often barely readable. Umbrella brands are still not prohibited in France as of early 2018.

Activox Rhume Pélargonium° oral solution (***Pelargonium root extract***) Arkopharma (Rev Prescrire n° 399)
For being part of an umbrella brand and for including the falsely reassuring statement in the patient leaflet that "*no interactions have been reported*", whereas *Pelargonium root extracts* contain coumarin derivatives and a risk of increasing the effect of oral anticoagulants has not been ruled out.

Delprim° tablets (***trimethoprim***) DB Pharma (Rev Prescrire n° 406)
For not giving due prominence to the INN on blister packs or sufficient information in the patient leaflet about the risks during pregnancy. The patient leaflet does not explain the risk of teratogenicity when *trimethoprim* is taken during the first trimester (neural tube closure defects, oral clefts, urinary tract abnormalities and congenital heart defects), and does not warn patients that exposure during the 3 months before pregnancy also seems to be associated with a higher incidence of congenital malformations.

Epclusa° tablets (***sofosbuvir + velpatasvir***) Gilead Sciences (Rev Prescrire n° 410)
For the bulk bottle and for providing insufficient information in the patient leaflet about adverse effects. The patient leaflet omits the known harms of *sofosbuvir* (arrhythmias, neutropenia, etc.) and most of the adverse effects that occurred during the clinical development of the *sofosbuvir + velpatasvir* combination, in particular: irritability, insomnia, rash, and depression.

PACKAGING THAT POSES A RISK OF DOSING ERRORS

Cosimprel° 5 mg/10 mg and 10 mg/5 mg tablets (***bisoprolol + perindopril***) Servier (Rev Prescrire n° 408)
For the strong visual resemblance between the labelling of the boxes and bulk bottles of these two combinations with "mirror-image" dose strengths (5 mg/10 mg and 10 mg/5 mg), which could cause dosing errors.

Kayexalate° powder for oral or rectal suspension (***sodium polystyrene sulfonate***) Sanofi Aventis (Rev Prescrire n° 407)
For failing to provide the means necessary for accurate dose preparation: multidose bulk jar with a spoon instead of single-dose sachets for adults; and no dosage form or dosing device suitable for children, necessitating extemporaneous preparation by a pharmacist. And for the lack of a child-proof closure on a jar containing such a large quantity of drug.

PACKAGING THAT POSES A RISK OF POISONING IN CHILDREN WHO INGEST THE CONTENTS UNNOTICED BY THEIR CARERS

Biocalyptol° **Biocalyptol Sans Sucre°** Zambon, **Dimétane°** Biocodex, **Hexapneumine Adultes°** **Hexapneumine Enfants°** Bouchara-Recordati, syrups (***pholcodine***) (Prescrire Int n° 184)
For the absence of a child-proof cap on the bottle of these 5 *pholcodine*-containing medicines, exposing children to the risk of serious adverse effects, in particular respiratory depression, if they accidentally ingest the contents.

Ferrostrane° syrup (***sodium feredetate***) Teofarma, **Fumafer°** chocolate-flavoured oral powder (***iron***) Sanofi Aventis (Rev Prescrire n° 405)
For marketing in France these two medicines for five decades in a bottle without a child-proof cap, exposing children to the risk of accidental ingestion of *iron* and its serious and potentially fatal adverse effects. As of early 2018, a child-proof cap has finally been added to Ferrostrane° bottles in France.

Nausicalm° syrup (***dimenhydrinate***) Nogues (Rev Prescrire n° 410)
For the absence of a child-proof cap on the bottle, exposing children to the risk of accidental ingestion of this antihistamine and its serious and potentially fatal adverse effects. In response to our query, the company informed us that a child-proof cap is planned for late 2018.

Colchicine Opocalcium° tablets (***colchicine***), **Colchimax°** tablets (***colchicine + opium powder + tiemonium***) Mayoly-Spindler (Rev Prescrire n° 402, Prescrire Int n° 187)
For lacking any specific safety features to make it harder for children to gain access to the tablets, which could result in a potentially fatal *colchicine* overdose. The box could have a safety catch, or the blister pack could have a child-resistant film, combined if necessary with a tool to help remove tablets.

▶ Translated from *Rev Prescrire* **February 2018**
Volume 38 N° 412 • Pages 86-87

2017 Prescrire Information Awards

The Information Awards focus on the information provided to Prescrire by the companies whose products we examined in the New Products section of our French edition in 2017.

HONOURS LIST
(in alphabetical order)

Outstanding:
– **EG Labo**

Followed by:
– Advicenne
– Arrow Génériques
– Bioprojet Pharma
– Delbert
– Medac
– Mylan
– Nordic Pharma

RED CARDS
(in alphabetical order)

– **Bristol-Myers Squibb**
– **Effik**
– **Genévrier**
– **Genzyme (Sanofi Group)**
– **Janssen Cilag**
– **Kyowa Kirin Pharma**
– **Menarini**
– **MSD**
– **Pfizer**
– **Swedish Orphan Biovitrum**
– **The Medicines Company**
– **UCB Pharma**

Quality of information from pharmaceutical companies

We use a 4-point scale to rate the quality of the information provided by companies in response to our systematic requests


Company provided detailed information including unpublished data and packaging items.

Company provided information limited to published regulatory data or packaging information.

Company provided minimal information, mainly regulatory and packaging information.


Company provided no information.

Pharmaceutical companies hold a wealth of information on the drugs they market or withdraw from the market. They have a responsibility to share this information, in part to help ensure that their drugs are used appropriately and to protect patients from adverse effects.

As part of its systematic literature search, *Prescrire* requests clinical data, packaging, and administrative and regulatory information from pharmaceutical companies, then compares them with information obtained from other sources.

Prescrire's Information Awards reflect how each company assumes its responsibility to share information.

Information requested from 101 companies in 2017. In 2017, we requested information from 101 pharmaceutical companies. Some companies chose to be transparent and demonstrated this by providing detailed, relevant information in response to *Prescrire*'s requests. These companies are placed on the Honours List (8 out of the 101 companies approached for information in 2017). Those rated as "Outstanding" provided us with particularly useful and detailed information without delay and sometimes without being asked (1 company, out of the 101 approached).

Other drug companies failed to respond to some or all of our requests for information, or provided only limited data. Some of them delayed their response and failed to provide usable information. Some omitted the most important or sensitive data. Red Cards are given to highlight persistent deficiencies in the provision of information by some drug companies (12 of the 101 approached).

Some of the other 81 companies provided a bare minimum of information, sending us only limited documentation, sometimes after several reminders. They avoided a Red Card by simply going through the motions of sharing information.

Still no improvement in 2017. The years go by, yet nothing changes. On the whole, pharmaceutical companies provide *Prescrire* with a lot of information, some new and some that we have already obtained elsewhere. But as in previous years, few pharmaceutical companies embraced transparency in 2017 by agreeing to share all the data they hold with the health professionals who subscribe to *Prescrire*.

▶ Translated from *Rev Prescrire* **February 2018**
Volume 38 N° 412 • Page 88