

1981-2008 : 28 years of Prescire Drug Awards

Translated from *Rev Prescire*
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The Prescire Drug Awards, Packaging Awards and Information Awards are carried out in total independence by Prescire editors (see Rules on www.prescire.org). They should be read in context of the review on new medicines in 2008 on pages 84-88.

The table opposite lists the drugs along with their initial ratings in the New Products section of the French edition of *la revue Prescire*. They are rated as follows:
B = Bravo
RA = Real Advance
OAA = Offers An Advantage

(1)	Pilule d'Or/Golden Pill	Honours list
1981 (n°10)	• VACCIN HEVAC B° (hepatitis B vaccine) (B)	• Androcur° (cyproterone) (RA) • Armophylline° (theophylline LP) (RA) • Cordium° (bepiridil) (RA) • Isoprinosine° (inosine acedoben dimepranol) (RA) • Pirlene° (pyrazinamide) (RA) • Tildiem° (diltiazem) (RA)
1982 (n°21)	(not attributed)	• Didronel° (etidronic acid) (RA) • Minirin° (desmopressin) (RA) • Nerfactor° (isaxonine) (RA)(2) • Vansil° (oxamniquine) (3)(RA)
1983 (n°31)	• LOPRIL° (captopril) (RA)	• Tigason° (etretinate) (RA)(3)
1984 (n°41)	(not attributed)	• Nizoral° (ketoconazole) (RA) • Orimetene° (aminoglutethimide) (RA) (3) • Ulcar° (sucralfate) (RA)
1985 (n°51)	(not attributed)	• Augmentin° (amoxicillin + clavulanic acid) (OAA)
1986 (n°61)	• ZOVIRAX° I.V. and tabs. (aciclovir) (B) and (RA)	• GHRH Clin Midy° (somatostatin) (RA) • Roacutane° (isotretinoin) (RA)
1987 (n°71)	• LUTRELEF° (gonadorelin) (B) • DECAPEPTYL° (triptorelin) (RA)	• Introna° (interferon alfa) (RA) • Moscontin° (sustained release morphine) (RA) • Zovirax° cream (aciclovir) (OAA) • Rifadine° (rifampicin) (RA) • Tegretol° (new indications) (carbamazepine) (RA)
1988 (n°81)	• LARIAM° (mefloquine) (B) • RETROVIR° (zidovudine) (B)	• Anexate° (flumazenil) (RA) • Nimotop° (nimodipine) (RA)
1989 (n°92)	• EPREX° (epoetin alfa) (B) • MECTIZAN° (ivermectin) (B)	• Malocide° (new indication) (pyrimethamine) (RA) • Nimotop° inj. (new indication) (nimodipine) (RA) • Sandostatin° (octreotide) (RA)
1990 (n°103)	(not attributed)	• Mopral° (omeprazole) (RA) • Narcan° (naloxone) (RA) • Pentacarinat° (pentamidine) (OAA)
1991 (n°114)	(not attributed)	• Aredia° (pamidronate) (RA) • Minirin° inj. (new indication) (desmopressin) (RA) • Levocarnil° (L-carnitine) (RA) • Sandostatin° (new indication) (octreotide) (RA)
1992 (n°125)	• SURFEXO° (pulmonary surfactant) (RA)(3)	• Apokinin° (apomorphine) (OAA) • Videx° (didanosine) (OAA)
1993 (n°136)	(not attributed)	• Avlocardyl° (new indication) (propranolol) (RA) • Daivonex° (calcipotriol) (OAA) • Sporanox° (itraconazole) (OAA)
1994 (n°147)	(not attributed)	• Botox°-Dysport° (botulinum toxin) (OAA) • Zophren° (new dosages) (ondansetron) (OAA)
1995 (n°158)	(not attributed)	• Methadone hydrochloride AP-HP° (methadone) (RA) • Retrovir° (new indication) (zidovudine) (RA) • Cogenate° - Recombinate° (recombinant factor VIII) (RA)
1996 (n°169)	• DIGIDOT° (antidigitalin antibodies) (B)	• Ceredase° (alglucerase) (RA) (3) • Normosang° (hemin arginine) (RA) • Subutex° (buprenorphine) (RA) • Zocor° - Lodalès° (new indication) (simvastatin) (RA) • Zeclar° - Naxy° (clarithromycin) ; Clamoxyl° - Gramidil° (amoxicillin) ; Mopral° - Zoltum° (omeprazole) ; Ogast° - Lanzor° (lansoprazole) (new indication) (RA)
1997 (n°180)	(not attributed)	• Elisor°-Vasten° (new indication) (pravastatin) (RA) • Novatrex° (new indication) (methotrexate) (OAA) • Vesanoïd° (new indication) (tretinoin) (RA)
1998 (n°192)	• CRIVIVAN° (indinavir) (RA)	• Cystagon° (cysteamine) (RA) • Viagra° (sildenafil) (RA)
1999 (n°203)	(not attributed)	• Sustiva° (efavirenz) (OAA) • NorLevo° (levonorgestrel) (OAA)
2000 (n°214)	(not attributed)	• Remicade° (infliximab) (OAA)
2001 (n°225)	(not attributed)	• Esterasine° (C1 esterase inhibitor) (RA) (3) • Trolovol° (new indication) (penicillamine) (RA)
2002 (n°236)	(not attributed)	• Replagal° (agalsidase alfa) (RA) (4) • Ceprotin°, Protexel° (human protein C) (RA) • Stromectol° (new indication) (ivermectin) (OAA)
2003 (n°247)	(not attributed)	• Carbaglu° (carglumic acid) (RA) • lVheBex° (hepatitis B immunoglobulin) (RA) • Meningitec° (conjugated meningococcal C vaccine) (OAA)
2004 (n°258)	(not attributed)	• Diacomit° (stiripentol) (OAA) • Fuzeon° (enfuvirtide) (OAA) • Morphine Aguettant° syrup (oral morphine) (OAA)
2005 (n°269)	(not attributed)	• Varivax° (chickenpox vaccine) (RA)
2006 (n°280)	• ORFADIN° (nitisinone) (B)	• Egaten° (tricyclazepam) (RA)
2007 (n°290)	• CARBAGLU° (carglumic acid) (a second look) (B)	• Glivec° (imatinib) (chronic myeloid leukaemia, a second look) (RA) • Herceptin° (new indication) (trastuzumab) (OAA)
2008 (n°302)	(not attributed)	No awards for any new products or new indications

1- Year and issue of the French edition *la revue Prescire* in which the Awards were published.
2- Now withdrawn from the French market, because of adverse effects.
3- No longer marketed in France.
4- New data led us to amend our rating (see *Prescire International* n° 67).



2008 Prescrire Drug Awards

The Prescrire Drug Awards focus on products evaluated during the previous year in the New Products section of our French edition (issues 291 to 302 in 2008).

Each month, the *Prescrire* editorial staff of presents systematic and comparative analyses of available data on newly approved drugs in France, and on new therapeutic indications approved for existing drugs. The aim is to help the reader distinguish, among the plethora of lavishly promoted new commercial products, those medications worth adding to their drug list or worth using instead of existing drugs.

This evaluation follows rigorous procedures (details on www.prescrire.org) that include a thorough literature search, a large panel of reviewers (specific to each project) and a quality control system to check that the text is consistent with the data in the references.

Independence. This work is carried out by the editorial staff in total independence. *Prescrire* is financed exclusively by individual readers' subscriptions, neither the French nor the English edition carries any paid advertising, nor do we receive grants or subsidies of any kind (see our annual financial report in each June issue).

At the end of each year, the Prescrire Drug Awards are based on the review articles published that year, and take into account any new data available since the initial articles were published.

The rules governing the Drug Awards are available on the *Prescrire* website at www.prescrire.org.

Therapeutic advance is defined as better efficacy, fewer or less severe adverse effects (for similar efficacy), or safer or more convenient administration.

2008: a few improvements in convenience only this year. In 2008, for the first time since the Drug Awards began in 1981, no drugs have been awarded the Golden Pill or mentioned on the Honours List (see above and page 80).

However, 3 products contributed to patient care through improved convenience.

In 2 cases, a substance with a well-known and clearly favourable risk-benefit balance (*metformin* and *methadone*) was marketed in an await-

Pilule d'Or/Golden Pill

The "Golden Pill" award is granted to drugs that provide a major therapeutic advance in a field in which no effective treatment was previously available.

NOT ATTRIBUTED IN 2008

Honours list

The drugs included on the Honours List provide a clear advantage for some patients in comparison to existing therapeutic options, albeit with certain limitations.

NO INCLUSIONS IN 2008



Noteworthy

The following drugs (in alphabetical order of their international nonproprietary names (INN), the drug's real name) made a modest contribution to patient care:

<i>metformin</i>	METFORMIN MERCK° dispersible tablets Mylan	1 st liquid oral form, as a dispersible tablet, of an essential drug for type 2 diabetes (<i>Prescrire International</i> 96)
<i>methadone</i>	MÉTHADONE AP-HP° capsules Bouchara-Recordati	1 st dry oral form (capsules) of opioid replacement therapy for opioid dependence, for patients already established on the oral solution form (<i>la revue Prescrire</i> 295 and coming in <i>Prescrire International</i>)
<i>urokinase</i>	ACTOSOLV° Eumedica	to clear thrombosed central venous catheters or dialysis catheters, after failure of <i>heparin</i> (<i>la revue Prescrire</i> 302 and coming in <i>Prescrire International</i>)

ed new pharmaceutical form. Although the packaging of the *methadone* capsules is particularly well designed (see page 82), considerable restrictions apply to access to this product in France.

The third case is a new indication for a thrombolytic agent (*urokinase*) marketed since the 1980s, in a situation where its use was already commonplace.

React. The paucity of new products providing even modest advantage stands in contrast to the increasing number of new products that expose patients to unjustified risks, as shown in the table on page 85. Above all, this seems to reflect the inadequacies of the licensing procedures and the failure

of the international system to encourage therapeutic advances.

There is an urgent need for the authorities (and pharmaceutical companies) to change course. It is up to patients and health professionals to see to it that it happens.

And it is in patients' and health professionals' interests to make best use in everyday practice of the qualities of the essential drugs on the market.

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2008 Prescrire Packaging Awards

The Packaging Awards focus on the packaging quality of drugs evaluated during the previous year in the New Products section of our French edition (issues 291 to 302 for 2008).



Packaging awards



- Méthadone AP-HP°** Bouchara-Recordati (*methadone*)
 For the pre-cut blister packs, with full labelling of each unit dose, protected with a tamper-proof film to minimise the risk of accidental ingestion, this morphine derivative being fatal at low doses in children. For the labelling that gives due emphasis to the international nonproprietary name (INN) and distinguishes clearly between the strengths, minimising the risk of error when preparing the doses (*la revue Prescrire* 295 and coming in *Prescrire International*).
- Miltex° cutaneous solution** Baxter (*miltfosine*)
 For the measures taken to guarantee safety at each step of dose preparation and when disposing of the packaging after administration of treatment: presence of a child-proof bottle, latex gloves and two waste disposal bags, drawing attention to the cytotoxic nature of the waste (*la revue Prescrire* 300).

The first aim of *Prescrire's* Packaging Awards is to draw the attention of healthcare professionals and patients to the dangers posed by certain types of drug packaging. They also promote examples of high-quality, patient-friendly packaging used by some pharmaceutical companies and encourage the others to improve their packaging.

Packaging that complies with all quality criteria receives a Packaging Award. Particularly poor packaging is awarded a yellow or red card, depending on how dangerous it is.

Systematic analysis throughout the year. Throughout the year the editorial staff examines the packaging of new drugs and of older drugs that have been modified. Every aspect is examined: the outer packaging (the box), the immediate packaging (blister pack, bottle, syringe, sachet, etc.), devices provided for preparing and/or administering the doses, and of course the package leaflet.

This systematic analysis is based on *Prescrire* standardised forms. The steps taken to guarantee the quality and safety of each item of packaging are studied, taking into account the risk-benefit balance of the drug, the patients concerned and the conditions of administration.

Total independence. A specialised team, the *Prescrire* packaging working group, produces an overview of the analyses. At the end of each year, the Packaging Awards are granted on the basis of the standardised forms, in total independence and with no input from drug or packaging manufacturers (rules available on www.prescrire.org).

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Yellow cards

- Actifed allergie cétirizine°** tablets McNeil Santé Grand Public (*cetirizine*)
 For the ambiguous labelling of this over-the-counter drug (belonging to an umbrella brand): the international nonproprietary name (INN) on the blister packs is particularly difficult to read and could lead to confusion with other drugs from the same umbrella brand (*la revue Prescrire* 296).
- Cymbalta°** capsules Lilly (*duloxetine*)
- Januvia°** tablets MSD-Chibret (*sitagliptin*)
- Xelevia°** tablets Pierre Fabre Médicament (*sitagliptin*)
 For the rather incomprehensible labelling (under the pretext of multilingualism): the unit doses are not fully and individually labelled, making it difficult to read the INN, especially if blisters are separated (*la revue Prescrire* 292, 295, 299).
- Maxalt°** tablets MSD-Chibret (*rizatriptan*)
 For the poorly legible labelling of the blister packs: unit doses are not fully and individually labelled, the INN is only marked once and in small characters (*la revue Prescrire* 300).
- Niquitin°** transdermal patches GlaxoSmithKline Santé Grand Public (*nicotine*)
- Testopatch°** transdermal patches Pierre Fabre Médicament (*testosterone*)
 For not featuring the name of the drug on the external surface of the patch, making it difficult to identify them once applied to the skin: this could cause confusion in the event of concomitant application of a similar patch (*la revue Prescrire* 293, 301).
- Vicks adultes toux sèche miel°** syrup Procter & Gamble Pharmaceuticals (*dextromethorphan*)
 For not supplying a dosing device with the syrup, which is available over the counter. Patients will therefore use a teaspoon, which can lead to dosing errors (*la revue Prescrire* 299).



Red cards

- Advilcaps°** soft capsules 200 mg and **Adviltab°** tablets 400 mg Wyeth Santé Familiale (*ibuprofen*)
 For insufficient information in the package leaflet on data suggesting an increased risk of miscarriage when NSAIDs are taken during the first trimester of pregnancy. This exposes pregnant women to an unjustified risk given how common its indications are (fever and pain) and the fact that these products are available over the counter (*la revue Prescrire* 301).
- Durogesic°** transdermal patches Janssen-Cilag (*fentanyl*)
 For the package leaflet which shows an illustration of a patch being applied to a child's chest. This site is too easily accessible to children. A child could remove and swallow the patch, and would be exposed to a potentially fatal overdose of *fentanyl* (*Prescrire International* 95, 96,98).
- Okimus°** tablets Biocodex (*quinine + hawthorn solid extract*)
 For the lack of a child-proof cap on the bottle; it is easy to open and contains tablets resembling chocolate sweets, creating a risk of massive ingestion which would be potentially fatal for young child (*la revue Prescrire* 297).
- Valda rhume°** tablets (*paracetamol + pseudoephedrine + vitamin C*) and **Valda toux sèche sans sucre°** oral solution (*pholcodine*) GlaxoSmithKline Santé Grand Public
 For the labelling of these two drugs from an umbrella brand illustrated with a plant, whereas they contain none: this trivialises the serious cardiovascular adverse effects of *pseudoephedrine* and the neurological adverse effects of *pholcodine* (especially as this oral solution is available over the counter) (*la revue Prescrire* 302).

2008 Prescrire Information Awards



The Information Awards focus on the quality of the information provided to *Prescrire* by the pharmaceutical companies whose products were evaluated in the New Products sections of our French edition during the previous year (issues 291 to 302 in 2008).

Prescrire's review articles dealing with new drugs and indications are based on a thorough literature search for documents relating to the drug's pre-approval assessment, especially clinical trial reports.

In addition to textbooks and bibliographic databases, the editorial staff searches the websites of drug regulatory agencies (a), health economics institutions, health technology assessment agencies and other institutions specialising in the relevant therapeutic field. We also search other independent journals belonging to the International Society of Drug Bulletins (ISDB), and any independent institutions that have evaluated the drug in question.

Assessing drug company transparency. We also question the companies that market each drug we analyse in France, to ensure that we take into account all the documents used to justify approval for marketing or to modify an existing marketing authorisation, including unpublished data. Such unpublished data (for example, clinical expert reports, trial summary tables, etc.) may be held by the drug regulatory agency that examined the marketing authorisation application and by the company that obtained marketing authorisation.

As with the other *Prescrire* Awards, a systematic and totally independent process is used to grant the Information Awards. The rules are available on our website www.prescrire.org.

Rewarding accountable companies. Some drug companies respond to our requests for information in a timely manner, providing us with detailed, relevant documentation, including unpublished data.

These companies are mentioned on the Honours List. Fewer generic manufacturers are featured in the list ever since *Prescrire* decided not to examine all new generics (b)(1).

The companies rated as Outstanding provided us with exhaustive and detailed information very quickly, sometimes without being asked.

Honours list (in alphabetical order)



- Outstanding : Bouchara-Recordati, Orphan Europe, Sanofi Pasteur MSD
- Followed by : Addmedica, Biocodex, Biogaran, Galderma, GlaxoSmithKline, Shire Human Genetic Therapies, Therakos Europe, Théramex

Red cards (in alphabetical order)



- Genévrier, Genopharm, Lilly, Sanofi Aventis, Servier, Takeda

What have the unhelpful companies got to hide? Other drug companies either fail to respond to our requests for information or provide only limited data. They tend to delay their reply for as long as possible, i.e. only after publication of the opinion of the French Transparency committee (that assesses the medical benefits of new drugs and advises on drug reimbursement), of the price in the *Journal Officiel* or after the launch of their advertising campaign. They may also omit the most relevant data, claiming to be too busy, that the administrative services are too slow or that the clinical data in question are confidential. Others withhold information as a kind of retaliation because they did not like one of our earlier product reviews.

Very few pharmaceutical companies persistently withhold information. For patients' sake, we hope that refusal of transparency and lack of respect for the independence of the editorial staff of *Prescrire* and for its subscribers are not their reasons for withholding information.

"Red cards" for withholding information are a way of highlighting persistent shortcomings in the provision of information by certain drug companies and a way of encouraging them to be more open.

Considering the transparency of the drug company when choosing a drug. A drug company's commitment to transparency is the fifth factor to be taken into account when choosing a drug, after its efficacy, adverse

effects, convenience and price. When two treatments are indistinguishable on the basis of these first four factors, then it is in patients' and healthcare professionals' best interests to select the product manufactured by a company that puts all its cards on the table and does not hide information about its products, including their limitations.

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a- Drug regulatory agencies release certain clinical and administrative data to health professionals and patients by publishing their public assessment reports, post-marketing follow-up data, detailed reasons for the changes made to marketing authorisations, and through rapid online publication of summaries of product characteristics (SPCs). The European Medicines Agency (EMA) still has some way to go in this area and the French Health Products Safety Agency (Afsaps) even more so (see this issue pages 84-88).

b- We continue to contact generic manufacturers to ask for administrative information, particularly about patents and marketing of generic drugs.

1- Prescrire Rédaction "Les copies du mois. Mieux faire face à l'avalanche de copies" *Rev Prescrire* 2007; 27 (280) : 106.

Each article examining a new drug is accompanied by a symbol (one of four) rating the transparency of drug companies in responding to our requests for information about their product (the rating system is explained on page 65).

