1981-2009 : 29 years of Prescrire Drug Awards

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The three annual Prescrire Awards, for drugs, packaging and information, are granted in total independence by Prescrire editors: the rules are available on our website, at www.english.prescrire.org. These Awards should be read in context of the review on new medicines in 2009 (see Prescrire's 2009 drug review, this issue page 76 and "A look back at 2009" page 89).

(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° (*bepridil*) (**RA**) • Isoprinosine° (*inosine acedoben dimepranol*) (**RA**) • Pirilene° (*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° (*somatorelin*) (**RA**) • Roaccutane° (*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)	• Apokinon° (*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**)(3)	• 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)	• **CRIXIVAN° (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**) • IVheBex° (*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° (*triclabendazole*) (**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
2009 (n°316)	(not attributed)	No awards for any new products or new indications

The table opposite lists the drugs along with their initial ratings in the New Products section of our French edition:
B = Bravo
RA = Real Advance
OAA = Offers An Advantage

1- Year and issue of the French edition *la revue Prescrire* 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 *Prescrire International* n° 67).

2009 Prescrire Drug Awards

Products evaluated during the previous year in the New Products section of our French edition are eligible for the Prescrire Awards for new drugs and indications (in 2009: issues 303 to 314).

Each month, the *Prescrire* editorial staff presents systematic and comparative analyses of available data on all newly approved drugs in France, and on new therapeutic indications granted for existing drugs. The goal is to help the reader distinguish, among the plethora of lavishly promoted commercial products, those medications worth adding to their drug list, or worth using instead of existing drugs. This evaluation follows rigorous procedures that include a thorough literature search, a large panel of reviewers (specific to each project) and a quality control system to verify that the text is consistent with the data in the references.

Total 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 *Prescrire International* 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 online, at www.english.prescrire.org.

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

2009: two minor advances. In 2009, as in 2008, none of the new drugs we examined was awarded the Golden Pill award or mentioned on the Honours List (see above and page 85).

However, two drugs that had already been on the market for several years were granted useful new indications. *Caspofungin*, an antifungal echinocandin, was approved as last resort therapy for some children with invasive aspergillosis, a rare but frequently fatal opportunistic infection. Clinical evaluation in this setting is still limited, but *caspofungin* is a welcome treatment option.

Thalidomide was approved for first-line treatment of multiple myeloma in patients over age 65. Two trials conducted by the same team showed that adding *thalidomide* to the standard *melphalan + prednisone* combination prolonged overall survival by at least 1.5 year in 50% of patients. However, three other trials showed no increase in overall survival; therefore, the precise survival benefit remains to be determined. *Thalidomide* has frequent and potentially severe adverse effects, including neuropathy and venous thrombosis. It is also highly teratogenic.

Stagnant situation. Once again, in 2009, the paucity of new products offering even a modest therapeutic advantage stands in stark contrast to the large number of new products exposing patients to unjustified risks: about 20 per year over the last 5 years (see pages 90 and 92).

The international system of incentives intended to encourage real therapeutic advances is clearly not working. There are also flagrant shortcomings in the marketing authorisation procedures and post-marketing pharmacovigilance.

If they are to regain the trust of patients and healthcare professionals, drug regulatory agencies and drug companies must shift the focus to more rigorous and more transparent clinical studies designed to meet important health needs.

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 AWARDED IN 2009

Honours list

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 2009

Noteworthy

The following drugs (in alphabetical order based on their international nonproprietary name (INN: " a drug's real name") made a modest contribution to patient care:

caspofungin	CANCIDAS° MSD-Chibret	Invasive aspergillosis in children in whom injectable *amphotericin* B and/or *itraconazole* is ineffective or poorly tolerated (*Prescrire Int* 102)
thalidomide	THALIDOMIDE CELGENE° Celgene	First-line treatment of multiple myeloma in selected patients over 65 years of age, in combination with *melphalan* and *prednisone* (*Prescrire Int* 100)

2009 Prescrire Packaging Awards

The Packaging Awards focus on the quality of packaging for drugs evaluated during the previous year in the New Products section of our French edition (2009: issues 303 to 314).

Packaging awards

NOT AWARDED IN 2009

Throughout the year, the editorial staff systematically examines the packaging of several hundred pharmaceutical products. This provides us with an opportunity to identify high-quality packaging and to detect dangerous packaging that is a potential source of confusion and errors, in order to inform our readers.

Detailed analysis. Every aspect of packaging is examined: the outer packaging (the box), the primary internal packaging (blister pack, bottle, syringe, sachet, etc.); devices provided for preparing and/or administering the doses; and of course, the legibility and quality of information provided in the package leaflet.

Specialised editors within the Prescrire Packaging Working Group further review packaging items and grant the annual Packaging Awards.

Annual Awards in total independence. At the end of each year, the Packaging Awards are granted following a review of the year's standardised forms, in total independence and with no input from drug or packaging manufacturers. The rules are available on our website, at www.english.prescrire.org.

No Awards granted in 2009. In 2009, as in previous years, the packaging of several products stood out from the rest for one reason or another (see the June 2010 issue). This year, however, none of them met all of the quality and safety criteria required to merit a Packaging Award.

Particularly poor packaging is awarded a yellow or red card, depending on the degree of risk it creates. Unfortunately, the list for 2009 is rather long (see right).

Yellow cards

• **Coversyl° tablets**, Servier ***(perindopril)***

• **Bipreterax° and Preterax° tablets**, Servier (***perindopril*** + ***indapamide***)

For the change in the way the *perindopril* dose is worded on the label, leading to a 20% increase in dosing specifications, even though the *perindopril* dose per tablet has barely changed. This represents a potential source of confusion and dosing errors. And for the switch from blister packs to bulk bottles without a childproof safety cap, creating a risk of overdose, especially in children (*Rev Prescrire* 313).

• **Vicks Expectorant adultes° syrup**, Procter & Gamble Pharmaceuticals ***(guaifenesin)***
For the poor legibility of the labelling information on the box; for example, the lack of contrast (white print on a metallic background) for useful information such as indications, making it difficult for patients to read the label and obtain the information they need for use of this over-the-counter medication (*Rev Prescrire* 306).

• **Tiorfanor° tablets**, Bioprojet ***(racecadotril)***
For the misleading promotional nature of the patient leaflet, which states that *racecadotril* is (our translation) "a very effective drug", while it provides no more than a limited reduction in stool frequency. This misleading claim may make patients neglect the need for rehydration (*Rev Prescrire* 307).

• **Betaine citrate Cristers° granules**, Cristers ***(betaine citrate)***
For minimising and scattering inadequate information printed on and inside the box (there is no proper patient leaflet), and the total lack of labelling on the sachets containing the granules, other than the lot number and expiry date (*Rev Prescrire* 311).

Red cards

• **Zarontin° syrup**, Pfizer (***ethosuximide***)
For the lack of dosing device in the box containing the bottle of this antiepileptic drug. The use of an ordinary spoon, as recommended in the patient leaflet, is a source of imprecise dosing, especially under-dosing, with a risk of seizure relapse (*Rev Prescrire* 309).

• **Nplate° powder for injectable solution**, Amgen (***romiplostim***)
For the ambiguous labelling of the "250 µg" dose strength (the bottle actually contains 375 µg of *romiplostim*), and the lack of a precise and appropriate dosing device. Together, these flaws represent a potential source of error during dose preparation. This is particularly problematic for an injectable drug that increases the platelet count (*Rev Prescrire* 311).

• **Prialt° 100 µg/1 ml and 500 µg/5 ml solution for intraspinal infusion**, Eisai (***ziconotide***)
For the inadequate information provided on the labelling: the total amount of *ziconotide* is not shown on the main face of the box, the INN is not mentioned on the bottle labels, and the words "solution for infusion" and "intraspinal route" are printed separately on the boxes. These represent sources of confusion that could lead to errors during dose preparation or in the choice of the route of administration (*Rev Prescrire* 312).

2009 Prescrire Information Awards

The Information Awards focus on the quality of the information provided to *Prescrire* by the pharmaceutical companies whose products we examined in the New Products section of our French edition during the previous year (in 2009: issues 303 to 314).

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, editors search 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 request relevant information from the companies that market each drug we analyse in France, to ensure that we take into account all documents, including unpublished data, used to justify marketing approval or to modify an existing marketing authorisation. Such unpublished data (for example, clinical reviews) may be held by the drug regulatory agency that examined the 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 (rules available on our website, at www.english.prescrire.org).

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

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

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

What do unhelpful companies have to hide? Other drug companies either fail to respond to our requests for information or provide only limited data. They tend to delay their response as long as possible, i.e. only after publication of the opinion of the French Transparency Committee (that assesses the comparative effectiveness of new drugs and provides advice on drug reimbursement), or 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.

Other companies withhold information as a kind of retaliation because they did not like one of our earlier product reviews. Few pharmaceutical companies persistently withhold information. For patients' sake, we hope that refusal of transparency or lack of respect for the independence of the editorial staff of Prescrire and its subscribers do not constitute 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 more openness.

Take into account drug company transparency 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 efficacy, safety, convenience and price. When two drugs are otherwise indistinguishable, then it is in patients' and healthcare professionals' best interests to select the product marketed by a company that puts its cards on the table and does not hide information, including the limitations of their products.

Honours list (in alphabetical order)

- Outstanding : **Janssen-Cilag and Sanofi Pasteur MSD**
- Followed by : **Bouchara-Recordati, EG Labo, GlaxoSmithKline, Leo, Mundipharma, and Nycomed**

Red cards (in alphabetical order)

- **Amgen, Bayer Schering, Lilly, Menarini, Pfizer, Sanofi Aventis, Servier, and Teva Pharma**

a- Drug regulatory agencies release some clinical and administrative data to healthcare professionals and patients by publishing their public assessment reports, post-marketing follow-up data, and detailed reasons for changes made to marketing authorisation, and through rapid online publication of summaries of product characteristics (SPCs). The European Medicines Agency (EMA) and the French Health Products Safety Agency (Afssaps) still have some way to go.

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

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

Whenever we examine a new drug, the article is accompanied by one of four pictograms rating the transparency of the company concerned for their response to our requests for information about their product (see this issue p. 67).