

1981-2010 : 30 years of Prescribe Drug Awards

Translated from *Rev Prescrire*
February 2011; 31 (328): 85-88



The three annual Prescribe 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 of new medicines (see “Enrichir et mettre à jour sa panoplie pour mieux soigner : le tri 2010 ?” *Rev Prescrire* 2011; 31 (327): 26-59, and “New drugs and indications in 2010: inadequate assessment; patients at risk”, in the April issue.

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)	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) • 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° (somatostatin) (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) • Sandostat° (octreotide) (RA)
1990 (n°103)	(not attributed)	• Mopral° (omeprazole) (RA) • Narcan° (naloxone) (RA) • Pentacarinate° (pentamidine) (OAA)
1991 (n°114)	(not attributed)	• Aredia° (pamidronate) (RA) • Minirin° inj. (new indication) (desmopressin) (RA) • Levocarnil° (L-carnitine) (RA) • Sandostat° (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)(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)	• CRIVAN° (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° (agalasidase 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 Aguetant° 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
2010 (n°328)	(not attributed)	Glivec° (imatinib) (inoperable and metastatic gastrointestinal stromal tumours, with more follow-up) (RA) see page 61

1- Year and issue of *la revue Prescrire* in which the annual awards were published.

2- Drug subsequently withdrawn from the French market because of adverse effects.

3- No longer marketed in France, as of 31 December 2010.

4- New data published after the inscription of this drug on the Honours List led us to revise our rating (see issue 241 p. 498-499).



2010 Prescribe Drug Awards

Products evaluated during the previous year in the New Products section of our French edition are eligible for the Prescribe Awards for new drugs and indications (in 2010: issues 315 to 326).

Each month, the *Prescribe* 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. *Prescribe* 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 *Prescribe International* June issue).

At the end of each year, the *Prescribe* 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.prescribe.org.

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

2010: only one major advance, and only for a few patients. As in 2008 and 2009, the Golden Pill Award was not attributed this year (see above and page 79). However, three drugs are worthy of note. *Imatinib* had already been on the market since 2002 for the treatment of inoperable or metastatic gastrointestinal stromal tumours. In the small number of patients concerned, after several years of follow-up, it has emerged that *imatinib* prolongs overall survival by more than 4 years, albeit at a cost of frequent and sometimes serious adverse effects. Its

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 2010		
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.		
<i>imatinib</i>	GLIVEC [®] Novartis Pharma	inoperable or metastatic gastrointestinal stromal tumours (a second look) (this issue page 61)
Noteworthy		
The following drugs (in alphabetical order of their international nonproprietary names – the INN is a drug's "real name") made a modest improvement in patient care:		
<i>azacitidine</i>	VIDAZA [®] Celgene	poor-prognosis myelodysplastic syndromes and related disorders in adults not qualifying for haematopoietic stem cell allografting (Prescribe Int n° 113)
<i>Japanese encephalitis vaccine</i>	IXIARO [®] Novartis Vaccines and Diagnostics	active immunisation of some adult travellers against Japanese encephalitis (Prescribe Int n° 106)



place as an adjuvant to surgical excision remains uncertain.

In some patients with poor-prognosis myelodysplastic syndromes and related disorders, adding *azacitidine* to symptomatic treatments prolongs overall survival by several months relative to standard cytotoxic drugs. But the assessment must continue, and haematological and gastrointestinal adverse effects must be taken into account.

Japanese encephalitis vaccine is useful for selected adults travelling to Asia in certain conditions. It is strongly immunogenic for at least a year, but we do not know how effectively it prevents clinical infections, or their accompanying sequelae and mortality. A risk of rare but serious adverse effects cannot be ruled out. This vaccine should be used with caution.

30 years of Prescribe Awards. Since 1981, only 14 new drugs have provided patients and caregivers with decisive advantages over existing options, sometimes reassessed after lengthy follow-up, or in indications other than those initially licensed. About 60 new drugs represented clear progress (see page 79). In recent years, however, about 20 commercial novelties are cluttering the market annually, and expose patients to unjustifiable risk. A good clean-out is needed.

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2010 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 (2010: issues 315 to 326).

Packaging Awards



NOT ATTRIBUTED IN 2010

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 (see in a coming issue of *Prescrire International*).

Detailed analysis. Every aspect of the 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.

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 by *Prescrire* Packaging Working Group, in total independence and with no input from drug or packaging manufacturers. The rules are available on our website, at www.english.prescrire.org.

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Yellow cards (in alphabetical order)



• **Exforge HCT° tablets** Novartis (**amlodipine 5 mg or 10 mg + valsartan 160 mg + hydrochlorothiazide 12.5 mg or 25 mg**)
For the similar labeling of the boxes and blister packs of different dose strengths, representing a source of confusion (Rev *Prescrire* n° 325).

• **Resikali° powder for oral or rectal suspension**
Fresenius Medical Care (**calcium sulfonate polystyrene**)
This product is not contained in a box, meaning that the information leaflet may be lost; in addition, the dosing spoon is buried within the powder and is sometimes difficult to find (Rev *Prescrire* n° 319).

• **Sifrol° LP sustained-release tablets** Boehringer Ingelheim (**pramipexole**)
For the ambiguous labeling of the blister packs (straddling two blisters), creating a risk of intake of two tablets instead of one (Rev *Prescrire* n° 323).

• **Temeritduo° tablets** Menarini (**nebivolol 5 mg + hydrochlorothiazide 12.5 mg or 25 mg**)
For the near-identical labelling of the boxes, representing a source of confusion between the dose strengths (Rev *Prescrire* n° 316 and 320).

Red cards



• **Codotussyl toux sèche enfants° and Codotussyl toux sèche adultes° (pholcodine) syrups** Génévrier
For the fanciful labelling of the boxes and bottles, overshadowing the international nonproprietary name (INN) and representing a source of confusion with other members of this over-the-counter umbrella range; also for the lack of safety cap, creating a risk of overdose in children (*pholcodine* has neurological adverse effects) (Rev *Prescrire* n° 317).

• **Coveram° tablets** Servier (**amlodipine 5 mg or 10 mg + perindopril 5 mg or 10 mg**)
For the bulk bottles that create a risk of overdose; and for the similar labelling of the different dose strengths, exposing patients to a risk of hypotension and malaise (Rev *Prescrire* n° 316).

• **Dolirhume aux huiles essentielles° solution for inhalation by fumigation** Sanofi Aventis (**Peru balm + eucalyptus and styrax tinctures + thyme and lavender essential oils + levomenthol**)
For the failure to mention the ingredients on the bottle, creating a source of medication errors; and for the lack of a safety cap, representing a risk of overdose in children (terpene derivatives can cause hallucinations, drowsiness and confusion) (Rev *Prescrire* n° 318).

• **Ebixa° oral solution** Lundbeck (**memantine**)
For the measuring device based on a primed pump, creating a risk of confusion and overdose and exposing patients to the adverse effects of this psychotropic drug (Rev *Prescrire* n° 323) (a).

• **Instanyl° nasal solution 50 µg, 100 µg or 200 µg per puff**
Nycomed (**fentanyl**)
For the unsafe packaging and the lack of a built-in mechanism ensuring a sufficient pause between puffs, thus creating a risk of overdose with this opiate (Rev *Prescrire* Int n° 110).

• **Keppra° oral solution 100 mg/ml** UCB (**levetiracetam**)
For the oral syringe graduated in milliliters of solution, requiring the user to convert the dose (in mg) to a volume (in ml), and representing a source of overdose with this antiepileptic drug used to treat children (Rev *Prescrire* n° 321 and 327).

• **Nurofenem° 400-mg tablets** Reckitt Benckiser (**ibuprofen**)
For the failure of the information leaflet to underline the risk of miscarriage linked to the use of nonsteroidal anti-inflammatory drugs (NSAIDs) during the first trimester of pregnancy. This exposes pregnant women to an unjustifiable risk with this widely used over-the-counter drug (Rev *Prescrire* n° 320).

• **Sodium valproate Winthrop 20 pour cent° oral solution (200 mg/ml)** Sanofi Aventis (**valproic acid**)
For the differences, relative to the reference product, in the graduation of the oral syringe, and the way in which the concentration is expressed on the box and bottle (b), creating a source of confusion and overdose, and exposing patients to an increased risk of adverse effects with this antiepileptic drug (Rev *Prescrire* n° 315).

• **VoltarenPlast° medicated plasters 140 mg**
Novartis Santé Familiale (**diclofenac**)
For the failure of the labeling and leaflet to underline cardiac and renal risks for the unborn child linked to the use of NSAIDs during the second trimester of pregnancy (Rev *Prescrire* n° 320).

a- After the review in Rev *Prescrire* n° 323, oral Ebixa° was modified.

b- Particularly as Depakine°, the reference product, is also marketed by Sanofi Aventis.

2010 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 2010: issues 315 to 326).

Prescrire's reviews 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, 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. We often request documents from drug regulatory agencies.

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 data, including unpublished data, used to justify marketing approval or to modify an existing marketing authorisation. Such unpublished data (for example, expert 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 data, including unpublished data. These companies are mentioned on the Honours List.

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

Honours list (in alphabetical order)



- **Outstanding :** Janssen-Cilag, Nycomed, Sanofi Pasteur MSD
- **Followed by :** CSL Behring, Galderma, GlaxoSmithKline and Lundbeck

Red cards (in alphabetical order)



- **Allergan, Génévrier, Ipsen, Lilly, Meda Pharma, Menarini, Pfizer, Pierre Fabre Médicament, Roche, Sanofi Aventis, Servier**

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 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 prefer the product manufactured by the company that has least to hide.

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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. 68).

