

1981-2004: 24 YEARS OF *PRESCRIBE* DRUG AWARDS



Prescrire's three yearly awards, for new drugs, packaging, and information, are granted in total independence by the *Prescrire* editorial team (rules available from www.prescrire.org). The awards should be seen in the context of "A review of new drugs in 2004" (in this issue pages 68-73).

The table opposite lists drugs analysed since 1981, along with the scores they were initially given in the New Products column of the French edition of this bulletin, *la revue Prescrire*. They are rated as follows:
B = Bravo
RA = Real Advance
OAA = Offers An Advantage

(1)	Golden Pill	Honours List
1981 (n°10)	• VACCIN HEVAC B° (<i>hepatitis B vaccine</i>) (B)	• Androcur° (<i>cyproterone</i>) (RA) • Armophylline° (<i>theophylline LP</i>) (RA) • Cordium° (<i>bepiridil</i>) (RA) • Isoprinosine° (<i>inosine acedoben dimepranol</i>) (RA) • Pirlene° (<i>pyrazinamide</i>) (RA) • Tildiem° (<i>diltiazem</i>) (RA)
1982 (n°21)	(not attributed)	• Didronel° (<i>etidronic acid</i>) (RA) • Minirin° (<i>desmopressin</i>) (RA) • Nerfactor° (<i>isaxonine</i>) (RA)(2) • Vansil° (<i>oxamniquine</i>) (3)(RA)
1983 (n°31)	• LOPRIL° (<i>captopril</i>) (RA)	• Tigason° (<i>etretinate</i>) (RA)(3)
1984 (n°41)	(not attributed)	• Nizoral° (<i>ketconazole</i>) (RA) • Orimetene° (<i>aminoglutethimide</i>) (RA) • Ulcar° (<i>sucalfate</i>) (RA)
1985 (n°51)	(not attributed)	• Augmentin° (<i>amoxicillin + clavulanic acid</i>) (OAA)
1986 (n°61)	• ZOVIRAX° I.V. and tabs. (<i>aciclovir</i>) (B) and (RA)	• GHRH Clin Midy° (<i>somatorelin</i>) (RA) • Roaccutane° (<i>isotretinoin</i>) (RA)
1987 (n°71)	• LUTRELEF° (<i>gonadorelin</i>) (B) • DECAPEPTYL° (<i>triptorelin</i>) (RA)	• Introna° (<i>interferon alfa</i>) (RA) • Moscontin° (<i>sustained release morphine</i>) (RA) • Zovirax° cream (<i>aciclovir</i>) (OAA) • Rifadine° (<i>rifampicin</i>) (RA) • Tegretol° (<i>carbamazepine</i>) (RA)
1988 (n°81)	• LARIAM° (<i>mefloquine</i>) (B) • RETROVIR° (<i>zidovudine</i>) (B)	• Anexate° (<i>flumazenil</i>) (RA) • Nimotop° (<i>nimodipine</i>) (RA)
1989 (n°92)	• EPREX° (<i>epoetin alfa</i>) (B) • MECTIZAN° (<i>ivermectin</i>) (B)	• Malocide° (new indication) (<i>pyrimethamine</i>) (RA) • Nimotop° inj. (<i>nimodipine</i>) (RA) • Sandostatin° (<i>octreotide</i>) (RA)
1990 (n°103)	(not attributed)	• Mopral° (<i>omeprazole</i>) (RA) • Narcan° (<i>naloxone</i>) (RA) • Pentacarinat° (<i>pentamidine</i>) (OAA)
1991 (n°114)	(not attributed)	• Aredia° (<i>pamidronate</i>) (RA) • Minirin° inj. (<i>desmopressin</i>) (RA) • Levocarnil° (<i>L-carnitine</i>) (RA) • Sandostatin° (<i>octreotide</i>) (RA)
1992 (n°125)	• SURFEXO° (<i>pulmonary surfactant</i>) (RA)(3)	• Apokinon° (<i>apomorphine</i>) (OAA) • Videx° (<i>didanosine</i>) (OAA)
1993 (n°136)	(not attributed)	• Avlocardyl° (<i>propranolol</i>) (RA) • Daivonex° (<i>calcipotriol</i>) (OAA) • Sporanox° (<i>itraconazole</i>) (OAA)
1994 (n°147)	(not attributed)	• Botox°-Dysport° (<i>botulinum toxin</i>) (OAA) • Zophren° (<i>ondansetron</i>) (OAA)
1995 (n°158)	(not attributed)	• Methadone hydrochloride AP-HP° (<i>methadone</i>) (RA) • Retrovir° (<i>zidovudine</i>) (RA) • Cogenate° - Recombinate° (<i>recombinant factor VIII</i>) (RA)
1996 (n°169)	• DIGIDOT° (<i>antidigitalin antibodies</i>) (B)	• Ceredase° (<i>alglucerase</i>) (RA) • Normosang° (<i>hemin arginine</i>) (RA) • Subutex° (<i>buprenorphine</i>) (RA) • Zocor° - Lodalès° (<i>simvastatin</i>) (RA) • Zeclar° - Naxy° (<i>clarithromycin</i>); Clamoxyl° - Gramidil° (<i>amoxicillin</i>); Mopral° - Zoltum° (<i>omeprazole</i>); Ogast° - Lanzor° (<i>lansoprazole</i>) (RA)
1997 (n°180)	(not attributed)	• Elisor°-Vasten° (<i>pravastatin</i>) (RA) • Novatrex° (<i>methotrexate</i>) (OAA) • Vesanoïd° (<i>tretinoin</i>) (RA)
1998 (n°192)	• CRIXIVAN° (<i>indinavir</i>) (RA)	• Cystagon° (<i>cysteamine</i>) (RA) • Viagra° (<i>sildenafil</i>) (RA)
1999 (n°203)	(not attributed)	• Sustiva° (<i>efavirenz</i>) (OAA) • NorLevo° (<i>levonorgestrel</i>) (OAA)
2000 (n°214)	(not attributed)	• Remicade° (<i>infliximab</i>) (OAA)
2001 (n°225)	(not attributed)	• Esterasine° (<i>C1 esterase inhibitor</i>) (RA) • Trolovol° (<i>penicillamine</i>) (RA)
2002 (n°236)	(not attributed)	• Replagal° (<i>agalsidase alfa</i>) (RA) (4) • Ceprotin°, Protexel° (<i>human protein C</i>) (RA) • Stromectol° (<i>ivermectin</i>) (OAA)
2003 (n°247)	(not attributed)	• Carbaglu° (<i>carglumic acid</i>) (RA) • IvheBex° (<i>hepatitis B immunoglobulin</i>) (RA) • Meningitec° (<i>conjugated meningococcal C vaccine</i>) (OAA)
2004 (n°258)	(not attributed)	• Diacomit° (<i>stiripentol</i>) (OAA) • Fuzeon° (<i>enfuvirtide</i>) (OAA) • Morphine Aguettant° syrup (oral morphine) (OAA)

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 score (see *Prescrire International* n°67).

The 2004 New Drug Awards

Products analysed during the past year in the New Products column of *la revue Prescrire* (issues 246 to 256 in 2004) are eligible for the annual New Drug Awards



The *Prescrire* awards for new drugs and indications are a rare opportunity to applaud new products released onto the French market that offer patients real therapeutic advantages.

Each month the editorial team presents systematic and comparative analyses of available data on all drugs newly marketed in France and on new therapeutic indications granted for existing drugs. The aim is to help the reader distinguish, among the plethora of lavishly promoted new commercial products (and despite the failings of the licensing authorities), those medications worth adding to their drug list or worthy of replacing existing drugs.

This analysis follows strict procedures (see www.prescrire.org) that include a thorough literature search, a large panel of reviewers (specific to each drug analysed), and a quality control system to check, among other things, that the text is perfectly congruent with the references.

Our work is financed exclusively by individual readers' subscriptions: neither the French nor English edition carries any paid advertising whatsoever, nor do we receive grants

or subsidies of any kind (see our yearly financial report in next issue).

All drugs analysed in the previous year's 11 issues of *la Revue Prescrire* are eligible for the New Drug Awards. Note that the selection process takes into account any new data published since the initial article was written. The editorial team confers the New Drug Awards, as well as the Information and Packaging Awards, in total independence. These awards are based solely on the results of a strict, systematic analysis aimed at

identifying major therapeutic advances for the patient. The rules governing the awards for new drugs are also available on the *Prescrire* website.

Therapeutic advance is defined as better efficacy, fewer or less severe adverse effects (for the same efficacy), or safer or more convenient administration. The 2004 New Drug Awards are granted to drugs meeting one or several of these criteria.

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Honours list

The following 3 drugs (in INN alphabetical order) provided a major advantage for some patients as compared with available treatments, though with some limitations.

enfuvirtide	FUZEON®	Combination therapy of HIV infected patients after multiple treatment failures with antiretrovirals (this issue page 60)	Roche
morphine liquid form	MORPHINE AGUETTANT® syrup	Ready to use for severe pain resistant to non opioid analgesics (la revue Prescrire n° 253)	Aguettant
stiripentol	DIACOMIT®	Severe myoclonic epilepsy in infants; reduces seizure frequency (this issue page 57)	Biocodex

Noteworthy

The following 4 drugs (in INN alphabetical order) made a more modest contribution to patient management.

atovaquone + proguanil	MALARONE® pediatric	Malaria prophylaxis in children in areas where <i>Plasmodium falciparum</i> is resistant to chloroquine (la revue Prescrire n° 255)	Glaxo-SmithKline
bosentan	TRACLEER®	Pulmonary arterial hypertension; no proven impact on survival, but offers a modest functional benefit (this issue page 47)	Actelion
laronidase	ALDURAZYME®	Replacement therapy of type I mucopolysaccharidosis in the least affected patients (Prescrire International n° 74)	Genzyme
topiramate	EPITOMAX®	Single-agent therapy in a few patients with refractory epilepsy; many adverse effects (Prescrire International n° 73)	Janssen-Cilag

Special award

This medicine was available under another name and used in the same indication, but packaging was not in line with use and approval was lacking. A new preparation is now available:

misoprostol	GYMISO®	Combined with mifepristone, for drug-induced abortion (la revue Prescrire n° 253)	HRA Pharma
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Golden Pill Award

Not awarded in 2004.

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

(the 12 drugs to have received this distinction over the last 24 years are listed in table on page 64).



2004 PACKAGING AWARDS

The Packaging Awards focus on the packaging quality of drugs evaluated during the previous year in the New Products column of our French edition (issues 246 to 256 in 2004).

La revue Prescrire's packaging Awards were created 14 years ago in order to draw patients' and health care professionals' attention to the fact that high-quality packaging is an important factor in safe and effective treatment. They also provide us an opportunity to

congratulate companies that design patient-friendly packaging, and to encourage other firms to improve their packaging.

Throughout the year the editorial team examines the packaging of all new drugs reviewed in the 11 monthly issues of *la Revue Prescrire*. They focus on the outer packaging (the box), the primary internal packaging (bottle, blister pack, tube, etc.), the patient information leaflet, and on any devices provided for administration such as spoons, graduated oral syringes, syringes and needles for injection. The unit doses are also evaluated for ease of use and patient safety (tablet divisibility, patch adhesiveness, etc.).

This analysis is based on the use of standardised forms. It focuses on drug identifiers (labelling, printing, colour coding), other items contributing to safety of use (safety stoppers, dose differentiation), and items helping to inform the patient (labels' wording, leaflet). The balance of benefits versus harm is taken into account, along with the categories of patients and caregivers most likely to use the drug. Detailed results of the editorial team's packaging analyses in 2004 can be found on our website, at www.prescrire.org.

At the end of the year the Packaging Awards are conferred on the basis of the information recorded on these standardised forms. The Packaging Awards, like the awards for new drugs and information are granted in total independence, with no input from any of the companies concerned (rules available from www.prescrire.org).

There are three types of Packaging Awards: those that praise high-quality packaging; "yellow cards" for packaging that creates a risk of confusion or misuse; and "red cards" for packaging that places patients in major danger.

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Packaging awards

FLUDARA® tablets (*fludarabine*) - Schering.

Double packaging, with nearly unit-dose blisters inserted in a vial, with a safety cap; help to prevent handling-related risks due to this cytotoxic agent (Prescrire International n° 75)

MORPHINE AGUETTANT® syrup (*morphine*) - Aguettant.

Quality dosing dispenser and patient-friendly labelling; contribute to safe administration of this potent opioid analgesic (la revue Prescrire n° 253)

RETROVIR® liquid form for infants (*zidovudine*) - GlaxoSmithKline.

Dosing dispenser well suited to newborns; clear and informative labelling that help identify this antiretroviral for children (la revue Prescrire n° 255)

TRANXÈNE® 50 mg tablets (*clorazepate*) - Sanofi-Synthelabo.

Fewer tablets per box; safe unit-dose blisters, difficult to break, which helps make this trivialized high-strength benzodiazepine less benign (la revue Prescrire n° 248)

Yellow cards for packaging

MICARDIS® 20 mg tablets (*telmisartan*) - Boehringer Ingelheim.

No unit-dose blister; poorly legible and confusing labelling, despite claims of multi-language and compliance aids (la revue Prescrire n° 250)

NORMISON® tablets (*temazepam*) - Genopharm.

Available in bulk bottles without safety cap, very easy to open (la revue Prescrire n° 250)

PAROXÉTINE MERCK® - Merck Génériques, PAROXÉTINE QUALIMED® - Qualimed, et PAROXÉTINE RATIOPHARM® - Ratiopharm (*paroxetine* for the three).

Available in bulk bottles, which contributes to trivialize use and favour massive ingestion (la revue Prescrire n° 251 and 248)

RENNIE® sugar free, tablets to be crunched (*calcium and magnesium carbonate*)

- Roche Nicholas

Available as sweet-like rolls, with transparent packaging to be hooked up on display shelves, just like in a supermarket; help trivialize this medicine (la revue Prescrire n° 250)

SPEEDIFEN® tablets (*ibuprofen*) - Zambon.

No international non-proprietary name (INN) on main side of box and blister; no identification of the tablets of this over-the-counter nonsteroidal antiinflammatory drug (la revue Prescrire n° 253)

Red cards for packaging

CONCERTA® LP sustained release tablets - Janssen-Cilag et RITALINE® LP capsules - Novartis (*methylphenidate* for the two).

This psychostimulant is available in bulk bottles for children, who can open safety cap and swallow a massive dose (la revue Prescrire n° 249)

2004 INFORMATION AWARDS

The Information Awards focus on the quality of information provided to *Prescrire* by the companies whose products were assessed in the previous year's New Products columns (issues 246 to 256 of French edition in 2004).



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

In addition to textbooks and classical bibliographic databases, we search the websites of drugs regulatory agencies, health economics institutions, health technology assessment agencies, and other institutions specialising in the relevant therapeutic field. We also consult other independent journals belonging to the International Society of Drugs Bulletins (ISDB) and any independent institutions which have carried out evaluations of the drug in question. The dates and nature of the literature search are described in detail at the end of each article.

Company readiness to answer Prescrire's requests. We also question the firms that market the drugs in France, to ensure that we take into account all documents, including unpublished data, used to justify marketing authorisation. The drug regulatory agency that licensed the product, and/or the applicant may also possess important unpublished data, including unpublished clinical trial reports.

Some drug regulatory agencies make all of these data publicly available, along with their assessment reports, while others attempt to hide behind a wall of secrecy. Note that the French drug regulatory agency is just starting to come out of its shell of secrecy, much like the European agency EMEA (see page 70).

Similarly, some firms willingly answered our requests for information, in a timely manner, providing us with all the data that were used to support the marketing application. These companies are found in the Honours list of the Information

Awards. Companies that answered our requests promptly and with particularly thorough and detailed information are awarded a special distinction. In 2004 one company was awarded a special distinction for transparency with its in-house pharmacovigilance data, an exceedingly rare and praiseworthy policy.

Blunt refusals and trickery. Other companies provide partial answers or simply fail to respond. Some "forget" or refuse to provide certain documents, citing pretexts such as "the regulatory affairs department is too busy", "administrative procedures are slow", "clinical data are confidential", or "the data are held by the parent company and are unavailable in France".

These firms are awarded "Red cards", sometimes accompanied by a special note describing the company's secretive behaviour. In 2004, a Red card was created for "sham information", identifying firms that pretend to provide useful information but are very slow and in the end fail

to provide any information of interest. These companies apparently hold Prescrire's 28 000 subscribers in utter contempt.

Thus, the Information Awards are intended to encourage firms with responsible information policies and to encourage the remainder to improve their policies, and to respect patients' and health care professionals' need for reliable information.

Independent and systematic. As with the other *Prescrire* awards, the Information Awards are granted at the end of each year, based on the scores given to each batch of information we receive. The scores are based on the timeliness of the response and on the quality of the documents (types, exhaustiveness, pertinence). The selection procedure is described in detail on our website (www.prescrire.org). These Awards, as with those for new drugs and packaging are conferred in total independence, with no input whatsoever from the companies concerned.

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Honours list (in alphabetical order)

Outstanding: BAXTER, GILEAD SCIENCES

Followed by: ARROW GENERIQUES, BIOGARAN, BOSTON SCIENTIFIC INTERNATIONAL, BOUCHARA-RECORDATI, GLAXOSMITHKLINE, LAPHAL DEVELOPPEMENT, NOVARTIS, NOVARTIS SANTE FAMILIALE, SANDOZ, SOCOPHARM, THERAMEX

Special award for communicating quality pharmacovigilance data: MAYOLY-SPINDLER

Red cards (in alphabetical order)

For deliberate retention of information: AVENTIS PASTEUR MSD, BEAUFOUR IPSEN, MEDIPHA SANTE, RATIOPHARM, SERVIER

For irregular communication of information: ABBOTT, CHIESI, PIERRE FABRE

For sham information: ALCON, PFIZER