Prescrire's ratings of new drugs in 2023: a brief review

● Therapeutic advances were rare, and mainly benefit cancer patients. Most newly authorised products or indications offered no advantages over existing options, and a few were more dangerous than beneficial, especially for children.

Every month, Prescrire publishes independent systematic reviews of recent developments in Europe's pharmaceutical market, including marketing authorisations granted for new active substances, new combinations, new pharmaceutical forms, and new indications. Our aim is to help subscribers identify those that advance patient care. We also keep a close eye on re-examinations of the harm-benefit balance of drugs already on the market, news on adverse effects, drug shortages, market withdrawals (instigated by pharmaceutical companies or regulatory authorities), and reintroduction of previously withdrawn drugs.

121 new marketing authorisations examined, first and foremost in the interest of patients. Prescrire rated 121 new marketing authorisations in 2023 (see the table on p. 101).

Thirty of these offered some degree of added benefit compared with existing treatments, at least for some patients. Ten of these 30 (i.e. 8% of all the new products or indications evaluated in our French edition in 2023) represented a notable advance (rated "Offers an advantage") and the remaining 20 (16%) a minimal advance (rated "Possibly helpful"). These results are typical of the pattern observed over the previous 9 years.

Once again, most of the new authorisations we analysed in 2023 (73, 60%) were rated "Nothing new". In 10 cases (8%), the harm-benefit balance could not be determined on the basis of the data available (rated "Judgement reserved"). Finally, 8 new authorisations (7%) were considered more dangerous than beneficial (rated "Not acceptable"), fewer than in the previous 9 years, but still too many.

A few notable advances in oncology. Seven of the 10 new active substances or combinations of substances that represented a notable advance in 2023 are used in various cancer settings (including haematological malignancies) in adults or children. Another substance was authorised for lowering toxic plasma levels of *methotrexate*, a cytotoxic drug authorised for use in certain cancers.

Authorisations too often rashly extended to include children. The only notable advances in paediatrics were the combination of *ivacaftor* + *tezacaftor* + *elexacaftor*, authorised for children with cystic fibrosis from 6 years of age, and *blinatumomab*, authorised for children with acute lymphoblastic leukaemia from 1 year of age. Some other paediatric extensions were authorised rashly: *dapagliflozin* in type 2 diabetes from 10 years of age; *dupilumab* in severe asthma from 6 years of age; and *teriflunomide* in multiple sclerosis from 10 years of age. The risk of serious adverse effects with these 3 drugs is too high, given that their efficacy is modest at best in some cases and has not been demonstrated in other cases.

New data with longer follow-up provide useful clarification. In 2023, we re-assessed the harm-benefit balance of 6 drugs because new data had become available. On re-evaluation, 3 of them were rated "Offers an advantage": *olaparib*, a cytotoxic drug authorised as "maintenance" therapy for certain advanced ovarian cancers after first-line chemotherapy (initially rated "Judgement reserved"); *osimertinib* (Tagrisso°) with more follow-up, in the treatment of certain lung cancers (initially rated "Nothing new"); and *ribociclib,* an antineoplastic drug authorised for use in certain breast cancers (initially rated "Not acceptable").

Some welcome measures improved patient care... In 2023, a few useful substances were reintroduced to the market in France with a national marketing authorisation: *aciclovir* eye ointment (Aciclovir Agepha°) for herpes keratitis; *lomustine* (Lomustine Medac°) for certain brain tumours; and *horse antilymphocyte immunoglobulin* (Atgam°) for certain patients with aplastic anaemia.

In 2023, the European Commission revoked the marketing authorisations of all medicines in Europe containing the opioid *pholcodine* (which until then had been used in cough) due to the risk of fatal anaphylaxis during anaesthesia containing a neuromuscular blocker in patients previously exposed to *pholcodine*.

... but pseudoephedrine is still authorised. In a less welcome development, in late 2023, the European Medicines Agency's (EMA) pharmacovigilance committee (PRAC) simply concluded from a review of the harm-benefit balance of oral medicines containing *pseudoephedrine* that their summaries of product characteristics (SmPCs) should be modified. And unfortunately in early 2024 the EMA's Committee for Medicinal Products for Human Use (CHMP) considered this measure sufficient. *Pseudoephedrine*, a sympathomimetic vasoconstrictor used in the common cold, with serious adverse effects linked to the vasoconstriction it causes, should be withdrawn from the market.

In summary. Compared with the number of new authorisations in 2023, those that advanced patient care were few and far between, and were the exception in fields other than oncology. Innovation and novelty are not synonymous with progress.

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Prescrire's ratings of new products and new indications over the past 10 years

PRESCRIRE'S RATING	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
BRAVO	1	0	0	0	0	0	1	0	0	0
A REAL ADVANCE	2	3	1	1	2	1	2	3	0	0
OFFERS AN ADVANTAGE	5	5	5	9	11	10	6	14	11	10
POSSIBLY HELPFUL	15	15	9	18	22	13	18	19	23	20
NOTHING NEW	35	43	56	45	50	61	55	51	63	73
JUDGEMENT RESERVED	10	6	5	4	5	9	17	12	13	10
NOT ACCEPTABLE	19	15	16	15	9	14	10	9	14	8
TOTAL	87	87	92	92	99	108	109	108	124	121

OFFERS AN ADVANTAGE

- *Blinatumomab* (Blincyto°) for first relapse of acute lymphoblastic leukaemia in children (*Prescrire Int* n° 248).
- *Glucarpidase* to reduce *methotrexate* plasma concentrations and toxicity associated with high-dose *methotrexate* (*Prescrire Int* n° 251).
- *Human normal immunoglobulin* (Octagam°) in dermatomyositis (*Rev Prescrire* n° 476).
- *Ivacaftor + tezacaftor + elexacaftor* (Kaftrio°) in cystic fibrosis with at least one F508del mutation from 6 years of age (*Prescrire Int* n° 249).
- *Nivolumab* (Opdivo°) in advanced oesophageal squamous cell carcinoma expressing the PD-L1 protein (*Prescrire Int* n° 251).
- *Olaparib* (Lynparza°) (with more follow-up) as "maintenance" therapy after first-line chemotherapy in certain advanced ovarian cancers (*Prescrire Int* n° 256).
- *Osimertinib* (Tagrisso°) (with more follow-up) as adjuvant treatment in certain lung cancers (*Prescrire Int* n° 245).
- *Pembrolizumab* (Keytruda°) in cervical cancer that has metastasised or after treatment failure (*Prescrire Int* n° 254).
- *Ribociclib* (Kisqali°) (with more follow-up) as an add-on to an aromatase inhibitor in certain breast cancers (*Prescrire Int* n° 255).
- *Ripretinib* (Qinlock°) as fourth- or subsequent-line treatment for gastrointestinal stromal tumours (*Prescrire Int* n° 251).

POSSIBLY HELPFUL

- *Avacopan* (Tavneos°) in certain types of polyangiitis (*Prescrire Int* n° 251).
- *Buprenorphine* (Buvidal°) in opioid substitution treatment (*Rev Prescrire* n° 482).
- *Dexamethasone* (various brands) in multiple myeloma (*Rev Prescrire* n° 473).
- *Difelikefalin* (Kapruvia°) in pruritus associated with chronic kidney disease (*Prescrire Int* n° 249).
- *Enfortumab vedotin* (Padcev°) as third- or subsequent-line treatment for urothelial carcinoma (*Prescrire Int* n° 252).
- *Evinacumab* (Evkeeza°) in homozygous familial hypercholesterolaemia (*Prescrire Int* n° 254).
- *Fludrocortisone* (various brands) in adrenal insufficiency or orthostatic hypotension (*Rev Prescrire* n° 482).
- *Lenacapavir* (Sunlenca°) in multidrug-resistant HIV-1 infection (*Prescrire Int* n° 252).
- *Lenvatinib + pembrolizumab* (Lenvima°, Keytruda°) in advanced or relapsed endometrial cancer (*Prescrire Int* n° 250).
- *Menotrophin* (Menopur°) in male or female infertility (*Rev Prescrire* n° 473).
- *Nirsevimab* (Beyfortus°) in the prevention of RSV infection in infants (*Prescrire Int* n° 254).
- *Nivolumab* (Opdivo°) in advanced gastric or oesophageal adenocarcinomas expressing the PD-L1 protein (*Prescrire Int* n° 251).
- *Odevixibat* (Bylvay°) in progressive familial intrahepatic cholestasis (*Prescrire Int* n° 247).
- *Olaparib* (Lynparza°) as adjuvant treatment for certain breast cancers with a *BRCA* mutation (*Prescrire Int* n° 256).
- *Tebentafusp* (Kimmtrak°) in metastatic uveal melanoma (*Prescrire Int* n° 253).
- *Trastuzumab deruxtecan* (Enhertu°) in HER2-positive gastric cancers after failure of *trastuzumab*-containing chemotherapy (*Prescrire Int* n° 257).
- *Trastuzumab deruxtecan* (Enhertu°) in relapsed metastatic breast cancer with low HER2 overexpression (*Prescrire Int* n° 253).
- *Trastuzumab deruxtecan* (Enhertu°) in metastatic HER2-positive breast cancer, after one prior line of anti-HER2 therapy (*Prescrire Int* n° 254).
- *RSVpreF vaccine* (Abrysvo°) during pregnancy to prevent RSV infection in the woman's child after birth (*Prescrire Int* n° 258).
- *Vutrisiran* (Amvuttra°) in polyneuropathy associated with transthyretin amyloidosis (*Prescrire Int* n° 253).

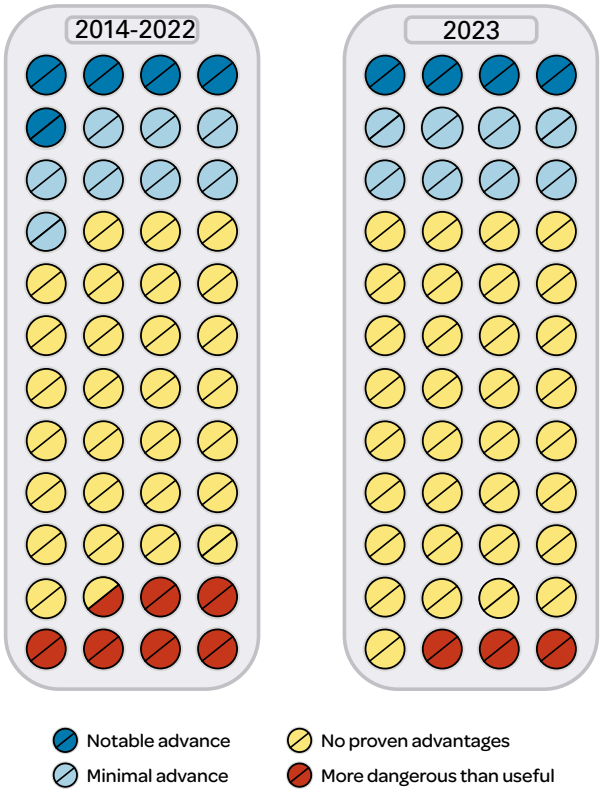
JUDGEMENT RESERVED

- *Abemaciclib* (Verzenios°) (with more follow-up) as an add-on to an aromatase inhibitor in certain breast cancers (*Prescrire Int* n° 255).
- *Axicabtagene ciloleucel* (Yescarta°) as second-line treatment in certain B-cell lymphomas (*Prescrire Int* n° 255).
- *Brexucabtagene autoleucel* (Tecartus°) in relapsed or refractory B-cell acute lymphoblastic leukaemia (*Prescrire Int* n° 258).
- *Burosumab* (Crysvita°) in tumour-induced osteomalacia (*Prescrire Int* n° 254).
- *Etilefrine* (Effortil°) in priapism (*Rev Prescrire* n° 482).
- *Eladocagene exuparvovec* (Upstaza°) in aromatic L-amino acid decarboxylase deficiency (*Prescrire Int* n° 255).
- *Idebenone* (Raxone°) (with more follow-up) in Leber hereditary optic neuropathy (*Prescrire Int* n° 251).
- *Pembrolizumab* (Keytruda°) after surgery in certain renal cancers *Prescrire Int* n° 259).
- *Pembrolizumab* (Keytruda°) after resection of melanoma at high risk of recurrence, and in certain adolescents (*Prescrire Int* n° 254).
- *Selumetinib* (Koselugo°) in plexiform neurofibroma due to neurofibromatosis type 1 (*Prescrire Int* n° 248).

NOT ACCEPTABLE

- *Dapagliflozin* (Forxiga°) in type 2 diabetes from 10 years of age (*Prescrire Int* n° 249).
- *Dupilumab* (Dupixent°) in severe asthma from 6 years of age (*Prescrire Int* n° 252).
- *Ozanimod* (Zeposia°) in ulcerative colitis (*Prescrire Int* n° 250).
- *Palbociclib* (Ibrance°) as an add-on to an aromatase inhibitor in certain breast cancers (*Prescrire Int* n° 255).
- *Risperidone* (Okedi°) in schizophrenia (*Prescrire Int* n° 252).
- *Teriflunomide* (Aubagio°) in multiple sclerosis from 10 years of age (*Prescrire Int* n° 253).
- *Upadacitinib* (Rinvoq°) in ulcerative colitis (*Prescrire Int* n° 254).
- *Vedolizumab* (Entyvio°) in pouchitis associated with ulcerative colitis (*Prescrire Int* n° 251).

Therapeutic advances in 2023 compared with the previous 10 years



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Prescrire's ratings

Our judgement is based on the therapeutic advance of the product in the relevant clinical situation. It considers not only the inherent value of each product in terms of its harm-benefit balance, but also its advantages and disadvantages relative to existing treatments. Note that the relative value of new products can vary from one country to another.

BRAVO
The product is a major therapeutic advance in an area where previously no treatment was available.

A REAL ADVANCE
The product is an important therapeutic advance but has certain limitations.

OFFERS AN ADVANTAGE
The product has some value but does not fundamentally change current therapeutic practice.

POSSIBLY HELPFUL
The product has minimal additional value, and should not change prescribing habits except in rare circumstances.

NOTHING NEW
The product is a new substance but with no evidence that it has more clinical value than other substances of the same group. It can be a me-too or a near me-too.

NOT ACCEPTABLE
Product without evident benefit but with potential or real disadvantages.

JUDGEMENT RESERVED
The editors postpone their rating until better data and a more thorough evaluation of the product are available.

Quality of information from pharmaceutical companies

In response to our systematic requests

The company provided detailed information, covering every aspect of our request.

The company provided information on every aspect of our request, but it was incomplete.

The company provided minimal information, or information obtainable elsewhere.

The company provided no information.