Drugs in 2018: a brief review

ABSTRACT

● **In 2018, 13 of the 99 new drugs, new dosages, new pharmaceutical forms or new indications analysed in our French edition constituted a notable therapeutic advance.**

● **The European Medicines Agency (EMA) sets the bar too low, especially for the evaluation of cancer drugs. The list of toxic, insufficiently evaluated drugs for multiple sclerosis continues to grow. "Orphan" drug status is particularly lucrative for pharmaceutical companies, yet only a minority of the new drugs or new indications with this status that we analysed in 2018 constituted a notable advance for patients.**

Every month, *Prescrire* publishes independent, comparative, systematic reviews of the latest developments in the pharmaceutical market: new active substances, new indications, new pharmaceutical forms. We also closely monitor drugs' adverse effects, market withdrawals (instigated by pharmaceutical companies or regulatory authorities), shortages, and the regulatory environment for health products, particularly at EU level. Our aim is to help subscribers distinguish between true advances in health care and new products or uses that are no better than existing treatments or should never have been authorised, due to uncertainty over their harms or benefits or because they are clearly dangerous.

In 2018, 99 new products or new indications were reviewed and rated in our French edition (see the table on p. 106). As in previous years, many did not advance patient care, with 50 being rated as "Nothing new". Of the 35 that did, 22 were a minimal advance (rated "Possibly helpful") and only 13 a notable advance (rated "A real advance" or "Offers an advantage"), including nasal *naloxone* for emergency treatment of opioid overdose, and a new drug, *sebelipase alfa* for the rare disease lysosomal acid lipase deficiency. In 5 cases, evaluation was insufficient to determine the harm-benefit balance of the drug in its authorised indications (rated "Judgement reserved"). Fewer new treatments than in previous years appeared more dangerous than useful (rated "Not acceptable").

This article draws attention to a few striking observations from 2018.

Drugs for multiple sclerosis: often highly toxic and poorly evaluated. In the Editorial p. 87 we reported on a study by an Italian team into the evaluation of the 10 drugs authorised for multiple sclerosis in the past 15 years. At the time of their market introduction, most of these drugs had only been compared with placebo, over a short period, and their effects on the longer-term progression of the disease were unknown. The many questions left unanswered were rarely resolved by the trials conducted after their authorisation (post-marketing studies).

This finding is consistent with *Prescrire*'s evaluations of drugs used in multiple sclerosis. They usually have immunosuppressant properties, little effect on progression of disability, and many severe adverse effects. Three of them (*alemtuzumab*, *natalizumab*, and *teriflunomide*) feature in *Prescrire*'s list of drugs to avoid, on account of their disproportionate harms (see p. 108).

In 2018, *Prescrire* analysed the evaluation data on three drugs authorised for multiple sclerosis: *daclizumab*, oral *cladribine*, and *ocrelizumab*. After analysing the initial evaluation of *daclizumab* and the serious and sometimes fatal harms already evident at this early stage, we concluded that it is more dangerous than useful (*Prescrire Int* n° 195). It is a typical example of a drug that should never have been authorised and in fact was subsequently withdrawn worldwide, but after much procrastination on the part of drug regulatory agencies and several patient deaths.

Prescrire also considered oral *cladribine* more dangerous than useful (*Prescrire Int* n° 196). In September 2018, the French pharmacoeconomic committee (Commission de la Transparence) came to a similar conclusion, rating *cladribine*'s therapeutic value "insufficient", which, at least in France, should reduce the number of patients exposed while it remains ineligible for reimbursement by the national health insurance system and unapproved for use in hospitals and other institutions.

As for *ocrelizumab*, *Prescrire* concluded that its harm-benefit balance is no better than *interferon beta* in the short term, and uncertain in the long term, in particular due to concerns over a possible risk of cancers (this issue p. 92).

"Orphan" drugs: lucrative for shareholders. As in previous years, "orphan" drugs accounted for a particularly high proportion of the drugs and indications newly authorised in 2018: 22 out of 99.

"Orphan" drug status has existed in the European Union since the year 2000, in theory to encourage research and development of drugs to improve the health of patients with rare diseases. In practice, they rarely constitute a real advance for these patients.

According to *Prescrire*'s analysis, 11 of the 22 new drugs or new indications we reviewed with this status in 2018 were an advance, but in most cases only a minimal advance. Only three constituted a notable advance: *sebelipase alfa* in lysosomal acid lipase deficiency was rated "A real advance" (*Prescrire Int* n° 200), and *everolimus* in epilepsy

Downloaded from english.prescrire.org on 09/05/2026
Copyright(c)Prescrire. For personal use only.

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

PRESCRIRE'S RATING	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
BRAVO	0	0	0	0	0	1	0	0	0	0
A REAL ADVANCE	0	1	0	1	0	2	3	1	1	2 (b)
OFFERS AN ADVANTAGE	3	3	3	3	6	5	5	5	9	11 (c)
POSSIBLY HELPFUL	14	22	13	14	12	15	15	9	18	22
NOTHING NEW	62	49	53	42	48	35	43	56	45	50
NOT ACCEPTABLE	19	19	16	15	15	19	15	16	15	9 (d)
JUDGEMENT RESERVED	6	3	7	7	9	10	6	5	4	5 (e)
TOTAL	104	97	92	82	90	87	87	92	92	99

a- This table includes new products (except copies) and new indications, as well as our updated reviews. The results for 1981 to 2008 are available (in French only) in *Rev Prescrire* n° 213 and *Rev Prescrire* n° 304.

For b, c, d, e:

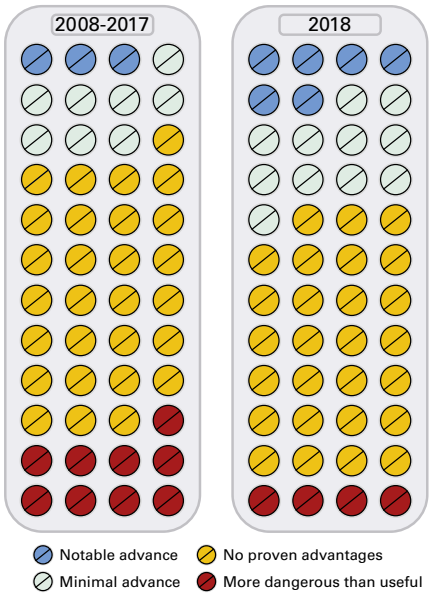
b- *sebelipase alfa* in lysosomal acid lipase deficiency (*Prescrire Int* n° 200) and nasal *naloxone* for emergency treatment of opioid overdose (*Prescrire Int* n° 199).

c-
- *arsenic trioxide* in acute promyelocytic leukaemia (*Prescrire Int* n° 193);
- *lidocaine + prilocaine* in premature ejaculation (*Prescrire Int* n° 197);
- *canakinumab* in periodic fever syndromes (*Prescrire Int* n° 198);
- *lopinavir + ritonavir* oral solution for HIV-infected children from 14 days of age (*Prescrire Int* n° 198);
- *everolimus* in epilepsy associated with tuberous sclerosis complex (*Prescrire Int* n° 199);
- *captopril* oral solution (*Rev Prescrire* n° 418);
- *etilefrine* in priapism (*Rev Prescrire* n° 420);
- *sofosbuvir* alone or combined with *ledipasvir* for adolescents with chronic hepatitis C (*Rev Prescrire* n° 421);
- *glecaprevir + pibrentasvir* in chronic hepatitis C (*Prescrire Int* n° 202);
- *midostaurin* in certain types of acute myeloid leukaemia (*Prescrire Int* n° 201);
- *sofosbuvir + velpatasvir + voxilaprevir* in chronic hepatitis C (this issue p. 89-91).

d-
- *dabrafenib* and *trametinib* combined for certain types of lung cancer (*Prescrire Int* n° 193);
- *pembrolizumab* in Hodgkin lymphoma with no further treatment options (*Prescrire Int* n° 195);
- *obeticholic acid* in primary biliary cholangitis (*Prescrire Int* n° 197);
- *daclizumab* in multiple sclerosis (*Prescrire Int* n° 195);
- *bezlotoxumab* for recurrence of *Clostridium difficile* infection (*Prescrire Int* n° 197);
- oral *cladribine* in multiple sclerosis (*Prescrire Int* n° 196);
- *olmesartan* for hypertension in children (*Prescrire Int* n° 199);
- *penicillamine* in lead poisoning (*Rev Prescrire* n° 418);
- *ribociclib* in locally advanced or metastatic breast cancer (*Prescrire Int* n° 202).

e-
- *lenalidomide* maintenance therapy in multiple myeloma (*Prescrire Int* n° 196);
- *eltrombopag* in chronic immune thrombocytopenia from 1 year of age (*Rev Prescrire* n° 416);
- *nusinersen* in spinal muscular atrophy (*Prescrire Int* n° 199);
- *avelumab* in metastatic Merkel cell carcinoma (*Rev Prescrire* n° 418);
- *dinutuximab beta* in neuroblastoma (*Prescrire Int* n° 201).

Therapeutic advances in 2018 compared with the previous 10 years



associated with tuberous sclerosis complex (*Prescrire Int* n° 199) and *midostaurin* in certain types of acute myeloid leukaemia (*Prescrire Int* n° 201) were both rated "Offers an advantage". One new "orphan" drug was considered more dangerous than useful and was added to *Prescrire*'s list of drugs to avoid (see p. 108): *obeticholic acid* in primary biliary cholangitis (*Prescrire Int* n° 197).

Insufficient data had been obtained to determine the harm-benefit balance of 4 new orphan drugs. This group included *nusinersen* for spinal muscular atrophy (*Prescrire Int* n° 199) for which, despite insufficient evaluation and uncertainty over its long-term effects, an exorbitant price was accepted by the French pharmacoeconomic authorities, at a cost to the national health insurance system of about 500 000 euros per patient for the first year of treatment, through a compassionate use programme (*Prescrire Int* n° 199).

Pharmaceutical companies that develop an orphan drug enjoy regulatory and financial benefits including an accelerated marketing authorisation process, market exclusivity for the first 10 years, and the possibility of conducting small and therefore generally less costly clinical trials. Some orphan drugs are subsequently authorised in several indications, extending their use and expanding their market share (*Prescrire Int* n° 171). For example, in 2018, *lenalidomide* was authorised for a third indication as an orphan drug, for patients with multiple myeloma (*Prescrire Int* n° 196), after previously being authorised as an orphan drug, for certain types of myelodysplastic syndrome and lymphoma. In 2015, *lenalidomide* was the ninth highest selling drug in the world, with global sales of 5.8 billion US dollars (*Prescrire Int* n° 196).

Cancer drugs: inadequate evaluation is becoming the norm. As in previous years, many (30/99) of the new products or indications we analysed in 2018 were from the field of oncology, only 11 of which were rated as an advance, and most of these were a minimal advance. Only 2 were notable advances: *arsenic trioxide* in acute promyelocytic leukaemia (*Prescrire Int* n° 193) and *midostaurin* in certain types of acute myeloid leukaemia (*Prescrire Int* n° 201 and 202).

Downloaded from english.prescrire.org on 09/05/2026
Copyright(c)Prescrire. For personal use only.

The European Medicines Agency (EMA) is clearly lowering the bar for drug evaluation and many cancer drugs are introduced on the market regardless of whether they constitute a therapeutic advance. It has become the norm to grant marketing authorisation on the basis of a single clinical trial, using laboratory or radiological endpoints that have not been proven to correlate with longer survival or better quality of life. The comparison is often inapropriate and non-blinded.

Typical examples include *elotuzumab* (*Prescrire Int* n° 193) and *ixazomib* (*Prescrire Int* n° 194) in multiple myeloma, *ofatumumab* (*Rev Prescrire* n° 411) in chronic lymphocytic leukaemia, and *alectinib* (*Rev Prescrire* n° 415) and *ceritinib* (*Rev Prescrire* n° 416) in certain types of lung cancer.

In some cases, the EMA is prepared to authorise drugs on the basis of non-comparative data, as it did with *venetoclax* for chronic lymphocytic leukaemia (*Prescrire Int* n° 198).

And however small the benefit to patients, new cancer drugs are sold by pharmaceutical companies at increasingly exorbitant prices (*Prescrire Int* n° 193).

In summary. In 2018, 13 of the 99 new drugs, new dosages, new pharmaceutical forms or new indications reviewed and rated in our French edition represented a notable advance for patients, a slight improvement on previous years.

However, the EMA's lax approach to drug authorisation is still in evidence, in particular in the field of cancer and in its inability to address the speculative use of incentives offered to encourage research into treatments for rare diseases. The exorbitant cost of some drugs jeopardises social protection systems and access to health care. Pharmaceutical company shareholders reap the benefits but at the expense of patients.

Review produced collectively by the Editorial Staff: no conflicts of interest

©Prescrire

▶ Translated from *Rev Prescrire* **February 2019**
Volume 39 N° 424 • Pages 142-144

COMING SOON...

NEW PRODUCTS

– Letermovir to prevent cytomegalovirus reactivation
– Pentosan polysulfate in bladder pain syndrome
– Cenegermin eye drops in neurotrophic keratitis

ADVERSE EFFECTS

– Angiotensin II receptor antagonists, also known as "sartans": psoriasis

REVIEWS

– Oral antihistamines and pruritus associated with skin disorders
– Unconjugated pneumococcal vaccine and COPD

OUTLOOK

– Drugs for Alzheimer's disease: reduction in the number of prescriptions too slow

Advancing healthcare policy

Via its policy advocacy, Prescrire acts as a force for change in health policies, first and foremost in the interest of patients. See the "Advancing healthcare policy" section of our website for a complete recap of Prescrire's policy advocacy actions, including this recent item:

• **EMA's opaque and confidential practice of early scientific advice (30 January 2019):**
In their joint response to the EU Ombudsman's consultation on the pre-submission "scientific advice" provided by EMA to pharmaceutical companies, ISDB and Prescrire argue that it is high time to put an end to EMA's opaque and confidential practice of early scientific advice and to take resolute action to promote independence and transparency.

See online at english.prescrire.org > Topics > Advancing healthcare policy

Downloaded from english.prescrire.org on 09/05/2026
Copyright(c)Prescrire. For personal use only.