Drugs in 2019: a brief review

● **Eleven of the 108 new drugs, combinations, dose strengths, pharmaceutical forms or indications analysed and rated in our French edition in 2019 constituted a notable therapeutic advance, improving patient care in a variety of fields (haemophilia, various cancers, HIV infection, hepatitis C and rare diseases).**

Every month, *Prescrire* publishes independent, comparative, systematic reviews of the latest developments in the pharmaceutical market, be they new active substances, new combinations, new dose strengths, new pharmaceutical forms or new indications. We also closely monitor news of 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.

11 notable advances among 108 new authorisations. In 2019, 108 new products or new indications were analysed and rated by *Prescrire* (see the table on p. 111). As in previous years, a high proportion did not advance patient care, with 61 rated as "Nothing new". Of the 24 that did, 13 represented a minimal advance (rated "Possibly helpful").

Only 11 constituted a notable advance (rated "A real advance" or "Offers an advantage"), 6 of which earned a 2019 Prescrire Drug Award. Nine had been too poorly evaluated to determine their harm-benefit balance (rated "Judgement reserved"). Finally, the data available on 14 of them showed that they are more dangerous than useful (rated "Not acceptable").

Few new drugs among the notable advances. Only two of the 11 notable advances in 2019, *emicizumab* and *durvalumab*, are new drugs. Two drugs, *trastuzumab emtansine* in certain types of breast cancer and *ruxolitinib* in myelofibrosis, were shown to be advances several years after their market introduction, in light of new data. Marketing authorisation is too often granted on the basis of grossly inadequate evaluation. Although the new data proved favourable to the drug in these two cases, the reverse can be true, with new data showing that patients have been unnecessarily exposed to a risk of serious adverse effects.

Chenodeoxycholic acid and *trientine* are old drugs that have only recently been granted marketing authorisation, a welcome development that facilitates access to these useful drugs and ensures they meet quality standards and are subject to surveillance.

Two products were authorised for a new age group: the *glecaprevir* + *pibrentasvir* combination for adolescents with chronic hepatitis C; and *raltegravir* for neonates with HIV infection, which was also marketed in new packaging to facilitate administration of the small doses required by babies.

In the field of oncology, two immunostimulants antibodies that act on the PD-1 receptor pathway advanced patient care: *pembrolizumab* in a new indication, and *durvalumab*, a new drug.

After cytotoxic drugs, endocrine therapy, targeted therapies and immunostimulants, 2019 saw the emergence of a new approach to the treatment of certain cancers in the form of CAR T-cell therapy, which is more akin to an autologous lymphocyte infusion than a drug. Although the results appear promising, the two CAR T-cell therapies now available, *axicabtagene ciloleucel* and *tisagenlecleucel*, have undergone only limited evaluation.

Positive action from the Transparency Committee of the French National Authority for Health. Two new drugs authorised in the EU were not examined in detail in *Prescrire* or rated in comparison with existing treatments for the same disease. The first is *olaratumab* (Lartruvo®), an antineoplastic authorised for the treatment of soft tissue sarcoma on the basis of woefully inadequate preliminary results, and its marketing authorisation was quite rightly withdrawn by the European Commission in mid-2019. The second is *padeliporfin* (Tookad®), a photosensitiser authorised for use in certain patients with localised prostate cancer, which has an uncertain harm-benefit balance (*Prescrire Int* n° 213). The Transparency Committee is safeguarding patients by issuing a negative opinion on funding of these two drugs by the national health insurance system, thus hindering their market introduction in France.

In summary: Prescrire's analyses are as necessary as ever. Only 10% of the new drugs, combinations, dose strengths, pharmaceutical forms and indications rated by *Prescrire* in 2019 constituted a notable therapeutic advance. Meanwhile, 20% had an uncertain, or even clearly unfavourable, harm-benefit balance. The European system for regulating the pharmaceutical market persists in favouring the pharmaceutical industry and in doing too little to protect patients. In this environment, *Prescrire*'s analyses and ratings remain as necessary as ever.

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

PRESCRIRE'S RATING	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
BRAVO	0	0	0	0	1	0	0	0	0	0
A REAL ADVANCE	1	0	1	0	2	3	1	1	2	1
OFFERS AN ADVANTAGE	3	3	3	6	5	5	5	9	11	10
POSSIBLY HELPFUL	22	13	14	12	15	15	9	18	22	13
NOTHING NEW	49	53	42	48	35	43	56	45	50	61
JUDGEMENT RESERVED	3	7	7	9	10	6	5	4	5	9
NOT ACCEPTABLE	19	16	15	15	19	15	16	15	9	14
TOTAL	**97**	**92**	**82**	**90**	**87**	**87**	**92**	**92**	**99**	**108**

A REAL ADVANCE

– *emicizumab* in patients with haemophilia A and factor VIII inhibitors (*Prescrire Int* n° 210).

OFFERS AN ADVANTAGE

– *chenodeoxycholic acid* in cerebrotendinous xanthomatosis (*Prescrire Int* n° 207);
– *glecaprevir* + *pibrentasvir* for adolescents with chronic hepatitis C (*Rev Prescrire* n° 434);
– *axicabtagene ciloleucel* in certain types of lymphoma when other treatment options have been exhausted (*Prescrire Int* n° 208);
– *durvalumab* as "maintenance" treatment in lung cancer (*Prescrire Int* n° 212);
– *pembrolizumab* in combination with cytotoxic drugs in lung cancers when a small proportion of tumour cells express the PD-L1 protein (*Prescrire Int* n° 212);
– *raltegravir* granules for neonates with HIV infection (*Rev Prescrire* n° 431);
– *ruxolitinib* in myelofibrosis (*Prescrire Int* n° 205);
– *tisagenlecleucel* for children and young adults with certain types of acute lymphoblastic leukaemia (*Prescrire Int* n° 208);
– *trastuzumab emtansine* in inoperable breast cancer (*Prescrire Int* n° 207);
– *trientine* in Wilson's disease (*Prescrire Int* n° 214).

POSSIBLY HELPFUL

– *emtricitabine* + *tenofovir disoproxil* for prevention of HIV infection in adolescents (*Prescrire Int* n° 206);
– *atazanavir* oral powder for patients from 3 months of age with HIV infection (*Prescrire Int* n° 207);
– *baclofen* in alcohol dependence (*Prescrire Int* n° 212);
– *cenegermin* eye drops in neurotrophic keratitis (*Prescrire Int* n° 204);
– *colchicine* in acute pericarditis (*Prescrire Int* n° 211);
– *dupilumab* in adults with atopic eczema (*Prescrire Int* n° 204);
– *erenumab* for prevention of migraine attacks (*Prescrire Int* n° 207);
– *glycopyrronium* for sialorrhoea due to neurological disorders (*Rev Prescrire* n° 430);
– *metreleptin* in lipodystrophy with leptin deficiency (*Rev Prescrire* n° 434);
– *pasireotide* for intramuscular use in Cushing's disease (*Rev Prescrire* n° 425);
– *peginterferon alfa-2a* for patients from 3 years of age with chronic hepatitis B (*Rev Prescrire* n° 423);
– *glycerol phenylbutyrate* in urea cycle disorders (*Rev Prescrire* n° 428);
– *tocilizumab* for subcutaneous use in giant cell arteritis (*Prescrire Int* n° 205).

JUDGEMENT RESERVED

– *adalimumab* in children with chronic anterior uveitis (*Rev Prescrire* n° 429);
– *brentuximab vedotin* in cutaneous T-cell lymphoma (*Rev Prescrire* n° 426);
– *burosumab* in X-linked hypophosphataemia (*Prescrire Int* n° 206);
– *cerliponase alfa* in neuronal ceroid lipofuscinosis type 2 (*Prescrire Int* n° 213);
– *darvadstrocel* for complex perianal fistulae in Crohn's disease (*Prescrire Int* n° 213);
– *mogamulizumab* in mycosis fungoides and Sézary syndrome (*Rev Prescrire* n° 434);
– *oxycodone* + *naloxone* in restless legs syndrome (*Prescrire Int* n° 205);
– *sirolimus* in sporadic lymphangioleiomyomatosis (*Prescrire Int* n° 212);
– *tocilizumab* in cytokine release syndrome due to CAR T-cell therapy (*Rev Prescrire* n° 428).

NOT ACCEPTABLE

– *abemaciclib* in certain types of breast cancer (*Rev Prescrire* n° 431);
– *colchicine* + *opium* + *tiemonium* in acute pericarditis (*Prescrire Int* n° 211);
– *ataluren* for children aged 2 to 4 years with Duchenne muscular dystrophy (*Prescrire Int* n° 213);
– *chondroitin* 1200 mg oral gel in sachets (*Rev Prescrire* n° 424);
– *ertugliflozin* in type 2 diabetes (*Prescrire Int* n° 213);
– *ethinylestradiol* + *dienogest* for contraception or acne (*Rev Prescrire* n° 426);
– *recombinant human parathyroid hormone* in chronic hypoparathyroidism (*Prescrire Int* n° 210);
– *mepolizumab* for patients from 6 years of age with severe asthma (*Prescrire Int* n° 211);
– *olaparib* in ovarian cancer without a BRCA mutation (*Prescrire Int* n° 209);
– *pentosan polysulfate* in bladder pain syndrome (*Prescrire Int* n° 204);
– *pertuzumab* as adjuvant treatment for certain types of breast cancer at high risk of recurrence (*Prescrire Int* n° 210);
– *solifenacin* oral solution in neurogenic detrusor overactivity in children (*Rev Prescrire* n° 429);
– *tenofovir alafenamide* + *emtricitabine* + *elvitegravir* + *cobicistat* for children with HIV infection (*Prescrire Int* n° 206);
– *tolvaptan* in polycystic kidney disease with severe renal failure (*Rev Prescrire* n° 431).

Therapeutic advances in 2019 compared with the previous 9 years