Prescrire's ratings of new drugs in 2021: a brief review

● Seventeen of the 108 new marketing authorisations analysed and rated in our French edition in 2021 represented a major or notable therapeutic advance for patients.

Every month, Prescrire publishes independent, comparative, systematic reviews of the latest developments in the European pharmaceutical market, including recent marketing authorisations for new active substances, new combinations, new dose strengths, new pharmaceutical forms and new indications (**a**). We also closely monitor news on adverse effects, market withdrawals (instigated by pharmaceutical companies or regulatory authorities), re-introductions of previously withdrawn products, new clinical evaluation data on drugs already on the market, shortages, and the regulatory environment for health products, particularly at EU level. Our aim is to help subscribers distinguish between genuine pharmaceutical advances and new products or new 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.

17 major or notable advances among 108 new authorisations. Prescrire analysed and rated 108 new marketing authorisations in 2021 (see the table opposite).

We noted a slight improvement in 2021 compared with the previous 5 years, with 36 of these new authorisations (about one-third of the reviews we published) offering some degree of benefit, at least for some patients. Three of them represented a major advance (earning the rating "A Real Advance") and 14 a notable advance (rated "Offers an Advantage"); five of the authorisations in these top two categories were for covid-19 vaccines. The remaining 19 of these 36 authorisations were minimal advances (rated as "Possibly Helpful").

As in 2020, about half of the authorisations we analysed in 2021 did not advance patient care (with 51 out of 108 rated "Nothing New"). Twelve had been too poorly evaluated to determine their harm-benefit balance (rated "Judgement Reserved"). Finally, the data available on 9 authorisations showed that they are more dangerous than useful (rated "Not Acceptable").

Two covid-19 vaccines and a drug used in acute hepatic porphyria are major advances. In 2021, two vaccines developed urgently in the midst of the covid-19 pandemic were major therapeutic advances: the messenger RNA vaccines *tozinameran* and *elasomeran*. In a completely different field, *givosiran,* a "small interfering" RNA, represented a major therapeutic advance for patients with acute hepatic porphyria, because it is highly effective at reducing the incidence of attacks, at least in the short term.

Most of the notable advances involved existing active substances. Two of the 14 notable advances were viral vector covid-19 vaccines authorised in the European Union: *covid-19 vaccine Ad26.CoV2-S* and *covid-19 vaccine ChAdOx1-S*.

Most of the other advances involved existing, sometimes rather old drugs, previously authorised for a different indication (e.g. *rituximab*, now authorised for pemphigus vulgaris), in a different pharmaceutical form (e.g. *budesonide*, now authorised in the form of orodispersible tablets for eosinophilic œsophagitis), or for a new route of administration (e.g. *glucagon* nasal spray). Three antiviral medicines used in hepatitis C, and already authorised for use in adults, were notable advances in the treatment of children: *sofosbuvir* alone, the combination of *sofosbuvir + ledipasvir*, and the combination of *sofosbuvir + velpatasvir*.

The reintroduction of fenfluramine, and a new amphetamine: drugs to avoid. The verdict in France's criminal trial involving the Mediator® disaster was delivered in 2021, with sentences for Servier, the company that marketed Mediator® (*benfluorex,* an amphetamine related to *fenfluramine*), and the French Health Products Agency. Yet the very same year, *fenfluramine* made a comeback, this time authorised for Dravet syndrome, a rare and serious form of infantile epilepsy. And a new amphetamine, *solriamfetol*, was authorised in the European Union for certain patients with excessive daytime sleepiness. Neither drug has a positive harm-benefit balance in the clinical situations for which they have been authorised, exhibiting limited efficacy and carrying the risks common to all amphetamines, in particular cardiovascular risks.

In summary. Three new drugs, all based on messenger RNA or small interfering RNA technology, represented a major therapeutic advance in 2021. But the bigger picture is that most of the new authorisations that advanced patient care were adaptations of existing drugs. And that more than half of this year's new authorisations were not advances, and in fact about one-tenth represented a step backwards compared to existing options.

α- *Prescrire International focuses on reviews related to marketing authorisations granted under the EU centralised procedure, and therefore does not publish all the reviews from the French edition.*

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

PRESCRIRE'S RATING	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
BRAVO	0	0	1	0	0	0	0	0	1	0
A REAL ADVANCE	1	0	2	3	1	1	2	1	2	3
OFFERS AN ADVANTAGE	3	6	5	5	5	9	11	10	6	14
POSSIBLY HELPFUL	14	12	15	15	9	18	22	13	18	19
NOTHING NEW	42	48	35	43	56	45	50	61	55	51
JUDGEMENT RESERVED	7	9	10	6	5	4	5	9	17	12
NOT ACCEPTABLE	15	15	19	15	16	15	9	14	10	9
TOTAL	82	90	87	87	92	92	99	108	109	108

A REAL ADVANCE

- The mRNA covid-19 vaccines *elasomeran* (Spikevax°) and *tozinameran* (Comirnaty°) in the prevention of covid-19 in adults (*Prescrire Int* n° 227).
- *Givosiran* (Givlaari°) in acute hepatic porphyria (*Prescrire Int* n° 227).

OFFERS AN ADVANTAGE

- *Atezolizumab* (Tecentriq°) in combination with *bevacizumab* in certain hepatocellular carcinomas (*Prescrire Int* n° 234).
- *Avelumab* (Bavencio°) in urothelial carcinoma (*Prescrire Int* n° 233).
- *Budesonide* (Jorveza°) in eosinophilic œsophagitis (*Prescrire Int* n° 234).
- *Eculizumab* (Soliris°) in neuromyelitis optica spectrum disorder (*Prescrire Int* n° 229).
- *Glucagon* (Baqsimi°) in hypoglycaemia with loss of consciousness (*Prescrire Int* n° 232).
- *Ivacaftor + tezacaftor + elexacaftor* (Kaftrio°) in cystic fibrosis with at least one F508del mutation (*Prescrire Int* n° 235).
- *Naloxone* (Nyxoid°) in opioid overdose (*Prescrire Int* n° 234).
- *Rituximab* (Mabthera° or other brands) in pemphigus vulgaris (*Prescrire Int* n° 226).
- *Rituximab* (Mabthera° or other brands) in severe polyangiitis in children (*Rev Prescrire* n° 456).
- *Sofosbuvir* (Sovaldi°), *sofosbuvir + ledipasvir* (Harvoni°) in chronic hepatitis C from 3 years of age (*Prescrire Int* n° 234).
- *Sofosbuvir + velpatasvir* (Epclusa°) in chronic hepatitis C in children from 6 years of age and in adolescents (*Prescrire Int* n° 234).
- The mRNA covid-19 vaccine *tozinameran* (Comirnaty°) in the prevention of covid-19 in adolescents (*Prescrire Int* n° 236).
- The viral vector *covid-19 vaccine Ad26.CoV2-S* (Covid-19 Vaccine Janssen°) in the prevention of covid-19 in adults (*Prescrire Int* n° 229).
- The viral vector *covid-19 vaccine ChAdOx1-S* (Vaxzevria°) in the prevention of covid-19 in adults (*Prescrire Int* n° 229).

POSSIBLY HELPFUL

- *Apalutamide* (Erleada°) in metastatic hormone-sensitive prostate cancer (*Prescrire Int* n° 230).
- *Apomorphine* in Parkinson's disease (*Rev Prescrire* n° 448).
- *Atezolizumab* (Tecentriq°) in small cell lung cancer (*Prescrire Int* n° 225).
- *Botulinum toxin type A* in urinary incontinence due to multiple sclerosis for patients able to void (*Rev Prescrire* n° 451).
- *Brimonidine* in glaucoma (*Rev Prescrire* n° 454).
- *Cabotegravir* (Vocabria°) in combination with *rilpivirine* (Rekambys°) in HIV infection (*Prescrire Int* n° 236).
- *Ciclosporin* eye drops (Verkazia°) in severe vernal keratoconjunctivitis (*Prescrire Int* n° 226).
- *Dapagliflozin* (Forxiga°) in chronic heart failure (*Prescrire Int* n° 232).
- *Docetaxel* (Taxotere° or other brands) in metastatic hormone-sensitive prostate cancer (*Prescrire Int* n° 231).
- *Encorafenib* (Braftovi°) in metastatic colorectal cancer with BRAF V600E mutation (*Prescrire Int* n° 232).
- *Enoxaparin* 12 000 and 15 000 units of anti-Xa activity (*Rev Prescrire* n° 454).
- *Erenumab* (Aimovig°) 140 mg in the prevention of migraine attacks (*Rev Prescrire* n° 453).
- *Etravirine* (Intelence°) in HIV infection in children aged 2 to 6 years (*Rev Prescrire* n° 454).
- *Gilteritinib* (Xospata°) in acute myeloid leukaemia with a FLT3 gene mutation (*Prescrire Int* n° 226).
- *Isatuximab* (Sarclisa°) in multiple myeloma (*Prescrire Int* n° 228).
- *Lidocaine* ophthalmic gel in local anaesthesia during ophthalmic procedures (*Rev Prescrire* n° 455).
- *Rituximab* (Mabthera° or other brands) in non-Hodgkin lymphoma in children (*Prescrire Int* n° 234).
- *Sevelamer* 0.8-g sachets (Renvela°) in hyperphosphataemia (*Rev Prescrire* n° 452).
- *Somatropin* in Noonan syndrome (*Rev Prescrire* n° 456).

NOTHING NEW

Among 108 new products or new indications, for 51 (47%) the analysis of the evaluation showed no contribution to an advance in patient care.

JUDGEMENT RESERVED

- Avapritinib (Ayvakyt°) in certain gastrointestinal stromal tumours (*Prescrire Int* n° 231).
- Belantamab mafodotin (Blenrep°) in multiple myeloma (*Prescrire Int* n° 230).
- Brentuximab vedotin (Adcetris°) in systemic anaplastic large cell lymphoma (*Rev Prescrire* n° 454).
- Brexucabtagene autoleucel (Tecartus°) in mantle cell lymphoma (*Rev Prescrire* n° 456).
- Bulevirtide (Hepcludex°) in chronic hepatitis D (*Prescrire Int* n° 230).
- Burosumab (Crysvita°) in X-linked hypophosphataemia in adults (*Prescrire Int* n° 235).
- Cefiderocol (Fetcroja°) in aerobic Gram-negative infections (*Prescrire Int* n° 236).
- Larotrectinib (Vitrakvi°) in cancers with an NTRK gene fusion (*Prescrire Int* n° 225).
- Lumasiran (Oxlumo°) in primary hyperoxaluria type 1 (*Prescrire Int* n° 234).
- Olaparib (Lynparza°) in combination with bevacizumab in ovarian cancer (*Prescrire Int* n° 234).
- Onasemnogene abeparvovec (Zolgensma°) in spinal muscular atrophy (*Prescrire Int* n° 231).
- Plerixafor (Mozobil°) in stem cell mobilisation for subsequent transplantation in children (*Rev Prescrire* n° 448)

NOT ACCEPTABLE

- *Atezolizumab* (Tecentriq°) in inoperable or metastatic triple-negative breast cancer (*Prescrire Int* n° 225).
- *Fenfluramine* (Fintepla°) in Dravet syndrome (*Prescrire Int* n° 233).
- *Fusidic acid + betamethasone* in infected atopic eczema (*Rev Prescrire* n° 451).
- *Nintedanib* (Ofev°) in systemic sclerosis-associated interstitial lung disease (*Prescrire Int* n° 231).
- *Nintedanib* (Ofev°) in various types of pulmonary fibrosis (*Rev Prescrire* n° 458).
- *Olaparib* (Lynparza°) in metastatic pancreatic cancer (*Prescrire Int* n° 230).
- *Omalizumab* (Xolair°) in nasal polyposis (*Prescrire Int* n° 232).
- *Siponimod* (Mayzent°) in secondary progressive multiple sclerosis (*Prescrire Int* n° 229).
- *Solriamfetol* (Sunosi°) in sleepiness due to narcolepsy or sleep apnoea (*Prescrire Int* n° 228)

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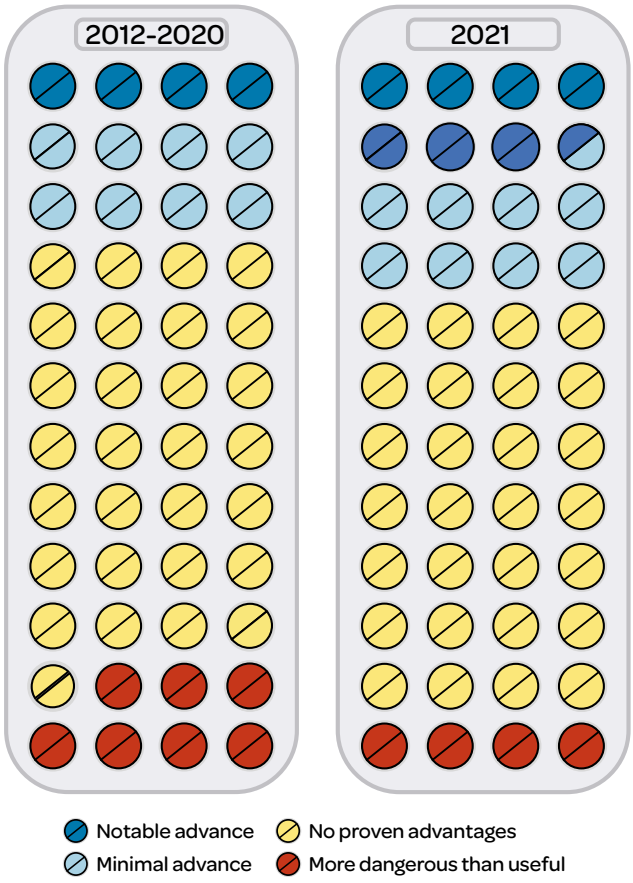
Therapeutic advances in 2021 compared with the previous 9 years



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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 the present 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

Company provided detailed information including unpublished data and packaging items.

Company provided information limited to published administrative data or packaging items.

Company provided minimal information, mainly administrative and packaging items.

Company provided no information.