

Main changes in the 2021 update

Prescrire updates its review of drugs to avoid every year. As a result, some drugs are added to the list, while others are removed, either because the pharmaceutical company or a health authority decided to withdraw the drug from the market, or pending the outcome of our re-assessment of the drug's harm-benefit balance, which may change in light of new data. Here we outline the main differences between the 2020 and 2021 lists of drugs to avoid.

Three drugs removed from the list of drugs to avoid. In 2019, we added **ulipristal** 5 mg (Esmya®) to the list of drugs to avoid, because this antagonist and partial agonist of progesterone receptors, used for uterine fibroids, can cause serious liver injury, sometimes requiring liver transplantation (*Prescrire Int* n° 198; *Rev Prescrire* n° 418) (a). Esmya's marketing authorisation was suspended in the European Union in March 2020 due to these serious hepatic effects, and in September 2020, the European Pharmacovigilance Risk Assessment Committee (PRAC) recommended withdrawal of its marketing authorisation.

The intestinal "anti-infective" agent **nifuroxazide** was also removed from our list of drugs to avoid, because it is supposedly no longer marketed in France. This drug has no proven efficacy against diarrhoea, but it provokes serious, albeit rare, immune-mediated and haematological adverse effects.

We also removed the antiangiogenic tyrosine kinase inhibitor **nintedanib** from the list while we assess its harm-benefit balance in two new indications added in 2020: chronic fibrosing interstitial lung diseases with a progressive phenotype, and systemic sclerosis-associated interstitial lung disease. *Nintedanib*'s harm-benefit balance remains unfavourable in the other situations for which it is authorised: idiopathic pulmonary fibrosis (*Prescrire Int* n° 173) and certain forms of non-small cell lung cancer (*Rev Prescrire* n° 389).

Gliflozins back on the list of drugs to avoid in diabetes. Glucose-lowering drugs belonging to the gliflozin class have been authorised for type 2 diabetes in the European Union since the mid-2010s. Increasing evidence of their unfavourable harm-benefit balance has accrued over time (*Prescrire Int* n° 160). Those currently marketed in

Europe are **canagliflozin** (alone or combined with *metformin*), **dapagliflozin** (alone or combined with *metformin* or *saxagliptin*), **empagliflozin** (alone or combined with *metformin* or *linagliptin*), and **ertugliflozin** (alone or combined with *metformin* or *sitagliptin*). Gliflozins were included in our 2019 list of drugs to avoid. They were removed in 2020 while we evaluated the harm-benefit balance of *dapagliflozin* in type 1 diabetes. *Dapagliflozin* has no more place in the treatment of type 1 diabetes than in type 2 diabetes. Following this re-evaluation, the gliflozin class of glucose-lowering drugs was reinstated on *Prescrire*'s list of drugs to avoid.

New drugs to avoid: finasteride 1 mg, piracetam, esketamine, etc. Two drugs were added to our 2021 list of drugs to avoid because their adverse effects are disproportionate when weighed against their weak efficacy or the benign condition for which they are authorised. They are **finasteride 1 mg**, authorised for use in men with male-pattern baldness, and the "vasodilator" **piracetam**, authorised for various clinical situations including vertigo and cognitive impairment.

Three other drugs have some efficacy, but their adverse effects are disproportionate or other, less dangerous options exist: **esketamine** nasal spray in "treatment-resistant" depression; **pimecrolimus** in atopic eczema; and **romosozumab** in severe postmenopausal osteoporosis.

Meloxicam joins the other nonsteroidal anti-inflammatory drugs (NSAIDs) on our list that belong to the oxicam class: *piroxicam* and *tenoxicam*. Its omission from last year's review was simply an oversight.

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► Translated from *Rev Prescrire* December 2020
Volume 40 N° 446 • Page 931

a- In postcoital contraception, ulipristal (still marketed under the brand name EllaOne®) is taken as a single 30 mg dose. Although it has not been shown to cause hepatitis when used in this way, levonorgestrel is a more cautious choice, especially since interactions between ulipristal and hormonal contraceptives can reduce the efficacy of ulipristal or the contraceptive (Prescrire Int n° 198 and n° 212).

112 authorised drugs that are more dangerous than beneficial

As of late 2020, based on the drugs examined by *Prescrire* between 2010 and 2020 that are authorised in France or in the European Union, 112 drugs were identified as more dangerous than beneficial in all their authorised indications. 93 of these drugs are marketed in France.

They are listed, based first on the therapeutic area in which they are used, and then in alphabetical

order according to their international nonproprietary names (INNs).

These 112 drugs comprise:

- Active substances with adverse effects that, given the clinical situations in which they are used, are disproportionate to the benefits they provide;
- Older drugs that have been superseded by newer drugs with a better harm-benefit balance;
- Recent drugs that have a less favourable harm-benefit balance than existing options;
- Drugs that have no proven efficacy beyond that