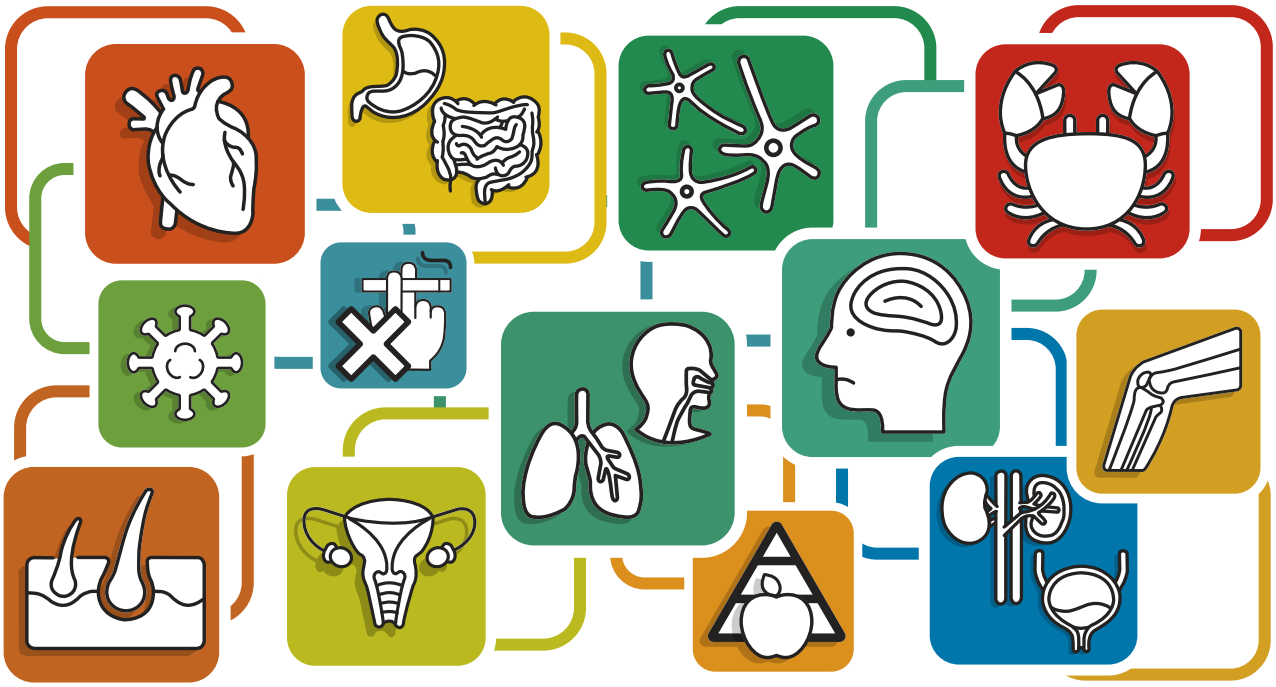

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Towards better patient care: drugs to avoid in 2026

● Prescrire's drugs to avoid is an annually updated review of drugs that are more dangerous than beneficial. It is intended as an aid to choosing high-quality care and preventing disproportionate harm to patients.

● Prescrire's assessment of a drug's harm-benefit balance in a given situation is underpinned by a rigorous procedure based on: a systematic and reproducible literature search; analysis of data on patient-relevant outcomes; prioritisation of the highest-level evidence; comparison with standard treatment, if one exists; and appraisal of the drug's known, foreseeable and suspected adverse effects.

● Our 2026 review of drugs to avoid covers all the drugs examined by Prescrire between 2010 and 2025 that are authorised in the European Union or in France. It consists of 108 drugs that have an unfavourable harm-benefit balance in all the clinical situations in which they are authorised.

● For the patients concerned, when drug therapy appears to be the best course of action, other options with a better harm-benefit balance are available. And in some situations, the most prudent option is to forgo drug therapy.

● Even when seriously ill patients have exhausted all other treatment options, there is no justification for exposing them to a drug with serious adverse effects when it has no demonstrated clinical efficacy. It may be acceptable to test such a drug in clinical trials, provided that the patients concerned are made fully aware of the uncertainties surrounding the drug's harm-benefit balance and the reasons for its continued evaluation, through discussions tailored to the patient's level of understanding. When such patients choose not to take part in a clinical trial, appropriate support and symptomatic care are called for, to mitigate the absence of any effective drug-based options capable of improving their prognosis or quality of life.

Prescrire Editorial Staff "Towards better patient care: drugs to avoid in 2026" *Prescrire Int* 2026; **35** (278): 54-55
(full version: 12 pages)

Prescrire International
A critical eye on new drugs authorised in Europe

Full review freely available at english.prescrire.org

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This is Prescrire's fourteenth consecutive annual review of drugs to avoid (1,2). It identifies drugs that are more dangerous than beneficial, providing supporting references, and is intended as an aid to choosing high-quality health care and preventing disproportionate harm to patients. The drugs cited (in rare cases, only a particular form or dose strength) should be avoided in all the clinical situations for which they are authorised in France or in the European Union.

What data sources and methodology do we use to assess a drug's harm-benefit balance?

A reliable, rigorous and independent methodology

Our 2026 review of drugs to avoid is based on the drugs and indications analysed in our French edition between 2010 and 2025. Some were examined for the first time, while others were re-evaluated as new data on efficacy or adverse effects became available.

One of Prescrire's main objectives is to provide health professionals (and thereby patients) with reliable, up-to-date information that is free from all conflicts of interest and supports high-quality health care.

Prescrire is structured in such a way as to guarantee the quality of the information provided to our subscribers. The Editorial Staff comprise a broad range of health professionals working in various sectors, with no conflicts of interest. We also call on an extensive network of external reviewers (specialists in the relevant area, methodologists, and practitioners representative of our readership), and each article undergoes multiple quality controls and cross-checking at each step of the editorial process (see About Prescrire > How we work at english.prescrire.org). Our editorial process is a collective one, as symbolised by the "©Prescrire" byline.

Prescrire is also fiercely independent. We are funded entirely by our subscribers, carry no paid advertising, receive no grants or subsidies of any kind, and have no shareholders. No company, professional organisation, insurance system or authority involved in the field of health care has any influence, financial or otherwise, over the content of our publications.

Comparison with standard treatments. A drug's harm-benefit balance and the choice of treatment options must be continually re-evaluated as new data on efficacy or adverse effects and new treatments become available.

Not all drugs are equal, and not all new drugs represent a clinical advance. Some drugs are useful in certain situations, offering a therapeutic advantage over other available treatment options, while other drugs are more dangerous than beneficial and should never be used (3).

Prescrire's assessments of drugs and indications are based on a systematic and reproducible literature search, and collective analysis of the resulting data by our Editorial Staff, using an established procedure:
– Efficacy data are ranked, with most weight given to those from studies that provide the highest level of evidence, i.e. double-blind randomised controlled trials;
– The drug is compared with the standard treatment (not necessarily a drug) when one exists, after determination of the best comparator;
– The efficacy results analysed are those that evaluate the clinical outcomes that matter most to the patients concerned (such as mortality, the most troublesome symptoms, or quality of life, depending on the situation), or surrogate outcomes (such as laboratory markers or imaging findings) that have been shown to correlate with relevant clinical outcomes (4,5).

Careful analysis of adverse effects. A drug's adverse effects can be more difficult to analyse, as they are often less thoroughly documented than its efficacy. This discrepancy must be taken into account when determining the drug's harm-benefit balance.

The adverse effect profile of each drug is assessed by examining the various signals that emerged during clinical trials and animal pharmacotoxicology studies, and by considering its pharmacological similarities to other drugs.

When a new drug is approved, many uncertainties remain. Some rare and serious adverse effects may not have been identified during clinical trials, and may only emerge after several years of routine use by a large number of patients (3).

Empirical data and personal experience: risk of major bias. Empirical assessment of a drug's harm-benefit balance, based on individual experience, can help to guide further research, but it is subject to major bias that strongly reduces the level of evidence of the findings (3,4). For example, it can be difficult to attribute a specific outcome to a particular drug, as other factors must be taken into account, including the natural history of the disease, the placebo effect, the effect of another treatment, or a change in diet or lifestyle. Similarly, a doctor who observes an improvement in certain patients cannot know how many other patients' conditions worsened when they received the same treatment (3).

The best way to minimise subjective bias caused by non-comparative, non-blinded evaluations in a small number of patients is to prioritise experimental data obtained in patients who agreed to participate in clinical trials, especially double-blind randomised trials versus standard care (3,4).

Serious conditions with no effective treatment: patients should be informed of the consequences of interventions. When faced with a serious condition for which there is no effective treatment, some patients opt to forgo treatment, while others are willing to try any drug if it offers the slightest chance of even temporary relief, despite a risk of serious adverse effects.

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But patients in this situation must not be treated as guinea pigs. Drug evaluations belong in the sphere of formal, properly conducted clinical research, not health care. It is of course useful to enrol patients in clinical trials, provided they are aware of the known or foreseeable risks and the uncertain nature of the possible benefits. And the results of these trials must be published in detail (whether positive, negative or inconclusive) in order to advance medical knowledge.

However, all patients must be offered the option of refusing to participate in a clinical trial or refusing a "last-chance" treatment with an uncertain harm-benefit balance. Even though support, attention and symptomatic treatments are not intended to cure or slow progression of the underlying disease, they are useful elements of patient care.

While a great deal of uncertainty surrounds the harm-benefit balance of drugs that are undergoing evaluation in clinical trials, drugs used for routine care must have a favourable harm-benefit balance. It is in the common interest that drugs should only be granted marketing authorisation on the basis of demonstrated efficacy relative to standard care, along with an adverse effect profile that is acceptable in the situation concerned, because in general, little if any additional information on efficacy is collected once marketing authorisation has been granted (3). And in the rare cases where drugs with an unfavourable harm-benefit balance are withdrawn from the market, it is a slow process.

108 authorised drugs that are more dangerous than beneficial

108 of the drugs examined by Prescrire between 2010 and 2025 that are authorised in France or in the European Union are more dangerous than beneficial in all their authorised indications (**a**).

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 108 drugs comprise:

– Substances with demonstrated efficacy but, given the clinical situations in which they are used, their adverse effects 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 demonstrated efficacy beyond that of a placebo, but that carry a risk of particularly severe adverse effects.

For each drug, we give the main reasons why it is considered to have an unfavourable harm-benefit balance, together with one or more Prescrire references where subscribers will find further details, including the external references on which our analysis was based. When better options are available, they are briefly mentioned, as are situations (serious or non-serious) in which there is no suitable treatment.

The differences between this year's and last year's versions are detailed in "Main changes in the 2026 update of Prescrire's drugs to avoid", p. 54-4.

Cardiology

• ***Aliskiren***, a blood pressure-lowering renin inhibitor, has not been shown to prevent cardiovascular events. Furthermore, a trial in diabetic patients showed that *aliskiren* was associated with an increase in cardiovascular events and renal failure (*Prescrire Int* n° 106, 129, 166, 184; *Rev Prescrire* n° 349). It is better to choose one of the many well-established blood pressure-lowering drugs, such as a thiazide diuretic or an angiotensin-converting enzyme (ACE) inhibitor.

• ***Andexanet alfa***, an antidote to anticoagulants of the direct factor Xa inhibitor (xaban) class, authorised for use in xaban-treated patients with severe bleeding, has not been shown to improve clinical outcomes. It exposes patients to an increased risk of thromboembolic events, in particular ischaemic stroke, and excess mortality has not been ruled out (*Prescrire Int* n° 217, 271).

• ***Bezafibrate***, ***ciprofibrate*** and ***fenofibrate*** are cholesterol-lowering drugs that have not been shown to prevent cardiovascular events. Yet they all have numerous adverse effects, including cutaneous, haematological and renal disorders (*Prescrire Int* n° 85, 117, 174). When the use of a fibrate is justified, *gemfibrozil* is the only one shown to have a degree of efficacy against the cardiovascular complications of hypercholesterolaemia, provided that renal function and serum creatine phosphokinase levels are closely monitored.

• ***Dronedarone***, an antiarrhythmic chemically related to *amiodarone*, is less effective than *amiodarone* at preventing atrial fibrillation recurrence. Yet it has at least as many severe adverse effects, in particular hepatic, pulmonary and cardiac disorders (*Prescrire Int* n° 108, 120, 122; *Rev Prescrire* n° 339). *Amiodarone* is a better option.

• ***Ivabradine***, a cardiac If current inhibitor, can cause visual disturbances, cardiovascular disorders (including myocardial infarction), potentially severe bradycardia and other cardiac arrhythmias. It has no advantages over other available options in either angina or heart failure (*Prescrire Int* n° 88, 110, 111, 118, 155, 165; *Rev Prescrire* n° 403, 413). Established treatments shown to be effective in angina include beta blockers or, as an alternative, calcium-channel blockers such as *amlodipine* and *verapamil*. There are also better options for heart failure, depending on the patient's situation, including refraining from adding another drug to an optimised treatment regimen.

a- *Nintedanib is mentioned twice in this review, in lung cancer (Vargetef°) and idiopathic pulmonary fibrosis (Ofev°), but has been counted as only one of the 108 drugs to avoid.*

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Main changes in the 2026 update of Prescrire's drugs to avoid

Prescrire updates its review of drugs to avoid every year, in the interest of improving patient care. The main differences between the 2025 and 2026 versions are outlined below.

Four new drugs to avoid: andexanet alfa, chondroitin, fezolinetant and gefapixant

These four drugs were added to Prescrire's 2026 edition of drugs to avoid due to their disproportionate adverse effects, given that they have no demonstrated clinical efficacy or that their efficacy is uncertain or too modest in comparison with placebo.

Andexanet alfa (Ondexxya°), an antidote to anticoagulants of the direct factor Xa inhibitor (xaban) class, authorised for use in xaban-treated patients with severe bleeding, carries a higher risk of serious thromboembolic events than usual care (*Prescrire Int* June 2025).

Chondroitin (various brands), an acid mucopolysaccharide used in some European countries in osteoarthritis although it has no demonstrated clinical efficacy, provokes sometimes serious adverse effects, including hypersensitivity reactions (erythema, urticaria or angioedema) (*Rev Prescrire* February 2025).

Fezolinetant (Veoza°), a drug intended to block neurokinin-3 (NK3) receptors, which are involved in thermoregulation, and that is authorised for menopause-related hot flushes, has disproportionate adverse effects including hepatotoxicity, gastrointestinal and neuropsychiatric disorders, as well as pain at various sites (*Prescrire Int* January 2026).

Gefapixant (Lyfnua°), an antagonist of the purinergic receptors P2X3 and P2X2/3, is the first drug to have been authorised in the European Union for patients with refractory or unexplained chronic cough. It carries a risk of very frequent taste disturbance, as well as pneumonia and urolithiasis (*Prescrire Int* November 2025).

Two drugs no longer included among Prescrire's drugs to avoid: obeticholic acid and piracetam

Obeticholic acid, a bile acid derivative formerly authorised in the European Union for primary biliary cholangitis as Ocaliva°, has been removed from the 2026 edition of drugs to avoid because its marketing authorisation has been revoked. It does not improve the health status of patients in this situation, when used either alone or in combination with *ursodeoxycholic acid*. It often exacerbates the main symptoms of the disease (pruritus and fatigue), and appears to carry a risk of serious and sometimes fatal hepatic adverse effects (*Prescrire Int* October 2018).

Piracetam (various brands), a "psychostimulant", is authorised in some European countries for use in various clinical situations, including vertigo, cognitive and neurosensory impairment in older adults, dyslexia in children, and myoclonus of cortical origin. On re-examining its harm-benefit balance in cortical myoclonus in 2025, the evaluation data showed it to have possible, but uncertain, clinical value in this rare situation (*Rev Prescrire* October 2025). As our review of drugs to avoid only includes drugs that are more dangerous than beneficial in all their approved indications, *piracetam* has been removed from this year's edition. Nevertheless, its harm-benefit balance remains unfavourable in its other authorised indications: its clinical efficacy has not been established, yet it carries a risk of haemorrhage, nervousness, agitation and weight gain (*Rev Prescrire* September 2020).

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Volume 45 N° 506 • Page 940

• ***Nicorandil***, a vasodilator with solely symptomatic efficacy in the prevention of effort angina, can cause severe mucocutaneous ulceration (*Prescrire Int* n° 81, 95, 110, 131, 132, 163, 175, 241; *Rev Prescrire* n° 336, 419). A nitrate is a better option for the prevention of angina attacks.

• ***Olmesartan***, an angiotensin II receptor blocker (ARB or sartan) marketed alone or in combination with *hydrochlorothiazide* or *amlodipine*, is no more effective than other ARBs against the cardiovascular complications of hypertension. However, it can cause sprue-like enteropathy leading to chronic diarrhoea (potentially severe) and weight loss, autoimmune hepatitis, and possibly an increase in cardiovascular mortality (*Prescrire Int* n° 148, 171, 242; *Rev Prescrire* n° 324, 374). Among the many other ARBs available, it is better to choose *losartan* or *valsartan*, which do not appear to have these adverse effects.

• ***Ranolazine***, authorised as an antianginal agent but with a poorly elucidated mechanism, has disproportionate adverse effects given its minimal efficacy in reducing the frequency of angina attacks, including: gastrointestinal disorders, neuropsychiatric disorders, palpitations, bradycardia, hypotension, QT prolongation and peripheral oedema (*Prescrire Int* n° 102; *Rev Prescrire* n° 350; *Interactions Médicamenteuses Prescrire*).

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• ***Trimetazidine***, a drug with uncertain properties that is used in angina, has no demonstrated efficacy beyond a modest effect on symptoms, shown mainly in stress tests. In a randomised placebo-controlled trial in 6000 patients with coronary heart disease who were followed up for several years, it was no more effective than placebo at preventing angina attacks. However, *trimetazidine* can cause parkinsonism, hallucinations, thrombocytopenia and drug reaction with eosinophilia and systemic symptoms (DRESS) (*Prescrire Int* n° 84, 100, 106, 266; *Rev Prescrire* n° 342, 357, 404, 457). It is preferable to choose treatments with a better-established harm-benefit balance in angina: certain beta blockers or, as an alternative, calcium-channel blockers such as *amlodipine* and *verapamil*.

• ***Vernakalant***, an injectable antiarrhythmic used in atrial fibrillation, has not been shown to reduce mortality or the incidence of thromboembolic or cardiovascular events. Its adverse effects include various arrhythmias (*Prescrire Int* n° 127). *Amiodarone* is a more prudent choice for pharmacological cardioversion.

Dermatology
Allergy

• **Oral *finasteride* 1 mg** and **topical *finasteride*** are authorised for androgenetic alopecia in men. Finasteride is a 5-alpha-reductase inhibitor with very modest efficacy in this situation. The oral form increases hair density on the crown of the head by about 10% on average, while the topical form adds about 13 extra hairs/cm^2 on average compared to placebo (from a baseline density of about 200 hairs/cm^2). The effect persists only while treatment continues, and hair density returns to baseline levels when treatment is stopped. Notable adverse effects include sexual dysfunction (erectile dysfunction, ejaculatory disorders, reduced sexual desire), depression, suicidal thoughts and breast cancer. These adverse effects are also possible when *finasteride* is applied topically (*Prescrire Int* n° 175, 196, 248, 275; *Rev Prescrire* n° 335, 503). When a pharmacological approach is chosen, topical *minoxidil*, used with caution, is less dangerous (**b**).

• ***Mequitazine***, a sedating antihistamine with antimuscarinic activity, authorised for allergies, has only modest efficacy. However, it carries a higher risk of cardiac arrhythmias through QT prolongation than other antihistamines, in particular in patients whose cytochrome P450 isoenzyme CYP2D6 metabolises the drug slowly (a characteristic that patients, doctors and pharmacists are generally unaware of), or when co-administered with drugs that inhibit CYP2D6 (*Rev Prescrire* n° 337). A "non-sedating" antihistamine without antimuscarinic activity, such as *cetirizine* or *loratadine*, is a better option in this situation.

• **Topical *pimecrolimus*** and **topical *tacrolimus***, two immunosuppressants used in atopic eczema, can cause skin cancer and lymphoma. These adverse effects are disproportionate, as the drugs' efficacy is barely different from that of high-potency topical corticosteroids (*Prescrire Int* n° 71, 101, 110, 118, 131, 224; *Rev Prescrire* n° 311, 331, 343, 367, 428) (**c**). Judicious use of a topical corticosteroid to treat flare-ups is a better option in this situation. There are almost no comparative evaluation data available on *pimecrolimus* or *tacrolimus* in patients in whom a topical corticosteroid has failed.

• **Injectable *promethazine***, an antihistamine used to treat severe urticaria, can cause thrombosis, skin necrosis and gangrene following extravasation or accidental injection into an artery (*Prescrire Int* n° 109). Injectable *dexchlorpheniramine*, which does not appear to carry these risks, is a better option.

• Powdered peanut seed, containing ***peanut protein***, taken orally to desensitise patients with peanut allergy, reduced the incidence and intensity of allergic reactions to peanuts in a test conducted in hospital. However, it increases the incidence of allergic reactions in patients' everyday life, including reactions that require *adrenaline* administration (*Prescrire Int* n° 238). In the absence of a better alternative, the first-choice measures are still a peanut-avoidant diet, as well as access to *adrenaline* injector pens, which patients as well as their carers should learn to use correctly.

Diabetes
Nutrition

Diabetes. Various glucose-lowering drugs have an unfavourable harm-benefit balance. They reduce blood glucose slightly, but have no demonstrated efficacy against the complications of diabetes (cardiovascular events, renal failure, neurological disorders), and have many adverse effects. The first-choice glucose-lowering drug for type 2 diabetes is *metformin*. If *metformin* alone is insufficiently effective, other options to consider include continued use of *metformin*, with the addition of: a subcutaneous GLP-1 agonist, such as *dulaglutide* or *semaglutide*; a gliflozin such as *dapagliflozin* for patients with heart failure or moderate renal impairment with proteinuria; or insulin if avoiding weight gain is not a priority. Another alternative is to raise the HbA1c target slightly.

• **Gliptins or DPP-4 inhibitors**, i.e. ***alogliptin***, ***linagliptin***, ***saxagliptin***, ***sitagliptin*** and ***vildagliptin***, have a burdensome adverse effect profile that includes serious hypersensitivity reactions (anaphylaxis and cutaneous reactions such as Stevens-Johnson syndrome), infections (in particular urinary tract and upper respiratory tract infections), pancreatitis, bullous pemphigoid, and intestinal obstruction

b- *Finasteride 5 mg is sometimes an option in benign prostatic hyperplasia, when alpha-1 blockers provide insufficient relief of urinary symptoms, are unsuitable or provoke unacceptable adverse effects (Prescrire Int n° 248).*

c- *Oral or injectable tacrolimus is a standard immunosuppressant for transplant recipients, a situation in which its harm-benefit balance is clearly favourable.*

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(*Prescrire Int* n° 121, 135, 138, 152, 158, 167, 186, 216; *Rev Prescrire* n° 349, 352, 354, 362, 365, 379, 473, 478).
• ***Pioglitazone*** also has a burdensome adverse effect profile, including heart failure, bladder cancer and bone fractures (*Prescrire Int* n° 129, 160).

Weight loss. The treatment of excess body weight usually primarily relies on changes to the patient's physical activity and diet, along with psychological support if necessary.
• ***Bupropion*** + ***naltrexone*** is a combination of a drug chemically related to certain amphetamines (*bupropion*) and an opioid receptor antagonist (see also *bupropion* in the Smoking cessation section of this article) (*Prescrire Int* n° 164, 262).
• ***Orlistat*** has only a modest and transient effect on weight: patients lost about 3.5 kg compared with placebo over 12-24 months, with no evidence of long-term efficacy. Gastrointestinal disorders are very common, while other adverse effects include liver damage, hyperoxaluria, and bone fractures in adolescents. *Orlistat* alters the gastrointestinal absorption of many nutrients (fat-soluble vitamins A, D, E and K), leading to a risk of deficiencies. It also reduces the efficacy of certain drugs (thyroid hormones, some antiepileptics). The severe diarrhoea caused by *orlistat* can reduce the efficacy of oral contraceptives (*Prescrire Int* n° 57, 71, 107, 110; *Interactions Médicamenteuses Prescrire*).

Gastroenterology

• **Medicinal clays**, i.e. ***beidellitic montmorillonite***, ***diosmectite***, ***hydrotalcite*** and ***kaolin***, used alone or in multi-ingredient products to treat various gastrointestinal disorders, including diarrhoea, heartburn and gastroesophageal reflux disease, should be avoided because they are naturally contaminated with lead. Lead has neurological, haematological, renal, cardiovascular and reproductive toxicity, and the severity of most of these toxic effects increases with the dose to which patients are exposed (*Prescrire Int* n° 203; *Rev Prescrire* n° 429, 430). In diarrhoea, clays alter stool appearance without reducing fluid loss or the consequent risk of dehydration. In uncomplicated gastroesophageal reflux disease, when pharmacological treatment seems helpful, other drugs have a positive harm-benefit balance, such as a short course of moderate doses of a clay-free antacid, e.g. *sodium bicarbonate* + *sodium alginate*.
• The neuroleptics ***domperidone***, ***droperidol*** and ***metopimazine*** carry a risk of arrhythmias and sudden death, and *domperidone* and *metopimazine*, at least, also carry a risk of ischaemic stroke. These adverse effects are disproportionate given the symptoms they are used to treat (nausea and vomiting, and gastroesophageal reflux in the case of *domperidone*) and their weak efficacy (*Prescrire Int* n° 129, 144, 175, 176, 179, 193, 230, 243, 265; *Rev Prescrire* n° 403, 404, 505). Other drugs have a favourable harm-benefit balance in gastroesophageal reflux disease, such as clay-free antacids or, when symptoms are severe or persistent, *omeprazole* for a few weeks at most, provided its discontinuation is planned from the outset, and that the patient is aware of the importance of switching to a different treatment if withdrawal symptoms occur. In the rare situations in which treatment with an antiemetic neuroleptic appears justified, *metoclopramide* has a better harm-benefit balance. *Metoclopramide* also provokes serious cardiac events, but has demonstrated efficacy against nausea and vomiting. It is essential, however, to keep exposure to a minimum, avoid continuous use, monitor patients frequently, and take interactions into account.
• ***Prucalopride***, a drug chemically related to neuroleptics, is authorised for chronic constipation but has only modest efficacy, and only in about one in six patients. Its adverse effect profile is poorly documented, and includes, in particular, cardiovascular disorders (palpitations, ischaemic cardiovascular events and possibly QT prolongation), depression, suicidal thoughts and teratogenicity (*Prescrire Int* n° 116, 137, 175). There is no justification for exposing patients with simple constipation to such risks. If dietary measures are insufficiently effective, bulk-forming laxatives, osmotic laxatives or, very occasionally, other laxatives (lubricants, stimulants, or rectal preparations), used carefully and patiently, are safer choices than *prucalopride*.
• ***Opium tincture***, a "soup" containing a variety of constituents of the poppy *Papaver somniferum* L., is authorised for severe diarrhoea. As an adjunct to rehydration, the opioid *loperamide* alone is a more prudent choice in this situation than a multitude of poppy-derived substances (*Rev Prescrire* n° 466).
• ***Glyceryl trinitrate* 0.4% ointment**, a nitrate authorised for anal fissure, has no demonstrated efficacy beyond that of a placebo in healing chronic anal fissures or alleviating the pain they cause. Headache is a very common adverse effect, and can be severe (*Prescrire Int* n° 94). Treatment of the pain associated with anal fissure is based on an oral analgesic such as *paracetamol* and sometimes topical *lidocaine*.

Gynaecology Endocrinology

Menopause. As of early 2026, for women experiencing very troublesome menopausal symptoms (including hot flushes, night sweats, vaginal dryness and atrophy), it is prudent to use only non-pharmacological measures, or to consider hormone replacement therapy for the shortest possible duration. Hormonal treatments should not be used in women at risk for thromboembolic events, or at increased risk of oestrogen-dependent tumours such as breast or endometrial cancer.
• ***Fezolinetant***, a drug intended to block neurokinin-3 (NK3) receptors, which are involved in thermoregulation, is authorised for menopause-related hot flushes but has very modest efficacy. It carries a risk of hepatotoxicity, gastrointestinal disorders,

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neuropsychiatric disorders, as well as pain at various sites. A possible increased risk of cancer should be taken into account (*Prescrire Int* n° 277).

• ***Tibolone***, a synthetic steroid hormone authorised in menopausal hormone replacement therapy, has androgenic, oestrogenic and progestogenic properties. Like oestrogen-progestogen combinations, it carries a risk of cardiovascular adverse effects and cancer (especially breast and endometrial cancer), but it has additional adverse effects due to its androgenic properties (*Prescrire Int* n° 83, 111, 137; *Rev Prescrire* n° 427).

Infectious diseases

• ***Moxifloxacin***, a fluoroquinolone antibiotic that is no more effective than other antibiotics of this class, can cause toxic epidermal necrolysis and fulminant hepatitis, and has also been linked to an increased risk of cardiac disorders (*Prescrire Int* n° 62, 103, 117; *Rev Prescrire* n° 371). Another fluoroquinolone such as *ciprofloxacin* or *ofloxacin* is a better option.

Neurology

Alzheimer's disease. The cholinesterase inhibitors authorised for use in Alzheimer's disease, as well as *memantine*, have minimal and transient efficacy in this situation, and none has been shown to slow progression toward dependence. They have serious and sometimes fatal adverse effects, and multiple, potentially dangerous, drug interactions, which are particularly problematic as these drugs are for long-term use (*Prescrire Int* n° 128, 150; *Rev Prescrire* n° 363). The priorities in the management of Alzheimer's disease are to help organise the patient's daily life, keep them active, and provide support and help for caregivers and family members. In France, when the national health insurance system stopped reimbursing these drugs, there was no increase in the number of consultations or rates of exposure to psychotropic drugs among patients who had previously been regularly exposed to at least one of these delisted drugs (*Prescrire Int* n° 228).

• The cholinesterase inhibitors ***donepezil***, ***galantamine*** and ***rivastigmine*** (**d**) can provoke gastrointestinal disorders (including sometimes severe vomiting), neuropsychiatric disorders (including depression and insomnia), anorexia, and cardiac disorders (including rhythm and conduction disorders, bradycardia, faintness and syncope). *Donepezil* can also cause compulsive sexual behaviour (*Prescrire Int* n° 162, 166, 192, 204, 243, 265; *Rev Prescrire* n° 337, 340, 344, 349, 398, 416).

• ***Memantine***, an NMDA glutamate receptor antagonist, can cause neuropsychiatric disorders (hallucinations, confusion, dizziness or headache), sometimes leading to violent behaviour, seizures, psychotic disorders, as well as heart failure or bradyarrhythmia (*Prescrire Int* n° 204, 225, 227; *Rev Prescrire* n° 359, 398).

Multiple sclerosis. The standard "disease-modifying" treatment for multiple sclerosis is *interferon beta*, despite its limitations and many adverse effects. The harm-benefit balance of the other "disease-modifying" treatments is no better and sometimes clearly unfavourable. This applies in particular to three immunosuppressants that have disproportionate adverse effects and should be avoided.

• ***Alemtuzumab***, an antilymphocyte monoclonal antibody, has uncertain efficacy and no demonstrated advantages over *interferon beta-1a*. It has many serious and sometimes fatal adverse effects, in particular: infusion-related reactions (including atrial fibrillation and hypotension), infections, frequent autoimmune disorders (including autoimmune thyroid disorders, immune thrombocytopenic purpura, cytopenia, nephropathy and hepatitis), myocardial infarction, pulmonary haemorrhage, stroke, and cervicocephalic arterial dissection (*Prescrire Int* n° 158, 218, 276; *Rev Prescrire* n° 384, 428).

• ***Natalizumab***, another immunosuppressive monoclonal antibody, can lead to potentially fatal opportunistic infections, including progressive multifocal leukoencephalopathy, potentially serious hypersensitivity reactions, and liver damage (*Prescrire Int* n° 122, 158, 182, 183, 276; *Rev Prescrire* n° 330, 464).

• ***Teriflunomide***, an immunosuppressant, has uncertain efficacy and no demonstrated advantages over *interferon beta-1a*. It has serious and potentially fatal adverse effects, including liver damage, leukopenia and infections. It also carries a risk of peripheral neuropathy (*Prescrire Int* n° 158, 253, 276; *Rev Prescrire* n° 482).

Miscellaneous. A number of other drugs used, in particular, in severe forms of epilepsy, migraine, cognitive impairment, vertigo, intermittent claudication and Parkinson's disease, should also be avoided.

• ***Fenfluramine*** is an amphetamine authorised as an add-on to antiepileptic therapy in Dravet syndrome and Lennox-Gastaut syndrome, two rare and serious forms of infantile epilepsy. Despite a decrease in the overall frequency of seizures, *fenfluramine* appears to increase the incidence of convulsive status epilepticus. *Fenfluramine* can provoke heart valve disease and pulmonary arterial hypertension, which is why its use as an appetite suppressant was discontinued. It can also cause neuropsychiatric disorders and other cardiovascular disorders (*Prescrire Int* n° 233, 263).

• ***Flunarizine*** and ***oxetorone***, two neuroleptics used to prevent migraine attacks, have at best only modest efficacy (*flunarizine* prevents about one attack every two months) and can cause extrapyramidal disorders, cardiac disorders and weight gain (*Rev Prescrire* n° 321, 359). *Oxetorone* also causes chronic diarrhoea (*Prescrire Int* n° 193). Other options, such as *propranolol*, are preferable.

d- *Rivastigmine also has an unfavourable harm-benefit balance in dementia associated with Parkinson's disease (Prescrire Int n° 265).*

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• ***Ginkgo biloba***, used in cognitive impairment in older adults, has no demonstrated efficacy beyond that of a placebo, but can cause haemorrhage, gastrointestinal disorders, skin disorders, seizures, hypersensitivity reactions and possibly arrhythmias (*Prescrire Int* n° 205, 224; *Rev Prescrire* n° 365). *Ginkgo biloba* is also used for venous insufficiency, as part of a fixed-dose combination with *heptaminol* and *troxerutin*, but its efficacy in this indication is no better (*Rev Prescrire* n° 413). There are no drugs with a favourable harm-benefit balance in these situations.
• ***Naftidrofuryl***, a "vasodilator" authorised for intermittent claudication associated with peripheral artery disease, increases walking distance by a few dozen metres, but it can cause headache, oesophagitis, mouth ulceration, skin disorders, kidney stones and potentially severe hepatic disorders (*Prescrire Int* n° 192; *Rev Prescrire* n° 427, 459). A walking exercise programme is an effective and less risky treatment.
• ***Tolcapone***, an antiparkinsonian COMT inhibitor, can cause life-threatening liver damage (*Prescrire Int* n° 82; *Rev Prescrire* n° 330). When other treatment options have been exhausted, *entacapone* is a better option.

Oncology Haematology

• ***Defibrotide***, an antithrombotic authorised for severe hepatic veno-occlusive disease following haematopoietic stem cell transplantation, was no more effective in reducing mortality or inducing complete disease remission than symptomatic treatment in a non-blinded trial, yet it provokes sometimes fatal haemorrhages (*Prescrire Int* n° 164). A more prudent option would be to focus on preventive measures and symptomatic treatments.

Antineoplastics. Various antineoplastic drugs have a clearly unfavourable harm-benefit balance. They are often authorised for situations in which other treatments seem ineffective. When exposure to highly toxic drugs is not justified by demonstrated benefits, it is prudent to focus on appropriate symptomatic care and on preserving quality of life.
• ***Mifamurtide*** is authorised in combination with other chemotherapy drugs for osteosarcoma, but it has not been shown to extend survival and can provoke serious hypersensitivity reactions, pleural and pericardial effusions, neurological adverse effects and hearing loss (*Prescrire Int* n° 115; *Rev Prescrire* n° 341). It is more prudent to propose chemotherapy without *mifamurtide*.
• ***Nintedanib***, a tyrosine kinase inhibitor with anti-angiogenic activity, authorised in combination with *docetaxel* for certain types of non-small cell lung cancer, has not been shown to extend survival. It can provoke liver injury and many severe adverse effects due to its inhibitory effect on angiogenesis, including venous thromboembolism, bleeding, hypertension, gastrointestinal perforation and impaired wound healing (*Prescrire Int* n° 173).
• ***Panobinostat*** has not been shown to prolong survival in refractory or relapsed multiple myeloma. It provokes many, often serious, adverse effects that affect vital functions, hastening the death of many patients (*Prescrire Int* n° 176).
• ***Roxadustat***, authorised for use in anaemia associated with chronic kidney disease, is no more effective in correcting anaemia than epoetins, overall, but it seems to increase mortality, especially in patients on dialysis. Its adverse effect profile appears similar to that of epoetins, but a number of potentially serious effects seem more frequent, in particular: thrombosis of vascular access (essential for performing dialysis), sepsis and hepatic disorders (*Prescrire Int* n° 245; *Rev Prescrire* n° 475). An epoetin remains a better option.
• ***Trabectedin*** was not shown to be effective in comparative trials in ovarian cancer or soft-tissue sarcoma, but it has very frequent and severe gastrointestinal, haematological, hepatic and muscular adverse effects (*Prescrire Int* n° 102, 115, 229; *Rev Prescrire* n° 360, 426). It is not reasonable to add *trabectedin* to platinum-based chemotherapy for ovarian cancer. When chemotherapy is ineffective in patients with soft-tissue sarcoma, it is more prudent to focus on symptomatic treatments in order to limit the clinical consequences of the disease.
• ***Vandetanib*** has not been shown to extend survival in patients with metastatic or inoperable medullary thyroid cancer. Serious adverse effects (diarrhoea, pneumonia, hypertension) occur in about one-third of patients. There is also a risk of interstitial lung disease, torsade de pointes and sudden death (*Prescrire Int* n° 131; *Rev Prescrire* n° 408).
• ***Vinflunine*** has uncertain efficacy in advanced or metastatic bladder cancer. A clinical trial provided weak evidence that *vinflunine* extends median survival by two months, at best, compared with symptomatic treatment. There is a high risk of haematological adverse effects (including aplastic anaemia), and a risk of serious infections and cardiovascular disorders (torsade de pointes, myocardial infarction, ischaemic heart disease), sometimes resulting in death (*Prescrire Int* n° 112; *Rev Prescrire* n° 360).

Pain Rheumatology

Certain nonsteroidal anti-inflammatory drugs. Although nonsteroidal anti-inflammatory drugs (NSAIDs) share a similar adverse effect profile, some expose patients to less risk than others. When *paracetamol* proves inadequate, the least risky options are *ibuprofen* and *naproxen*, provided that exposure is kept to a minimum and continuous use is avoided.
• **Oral *aceclofenac*** and **oral *diclofenac*** cause more cardiovascular adverse effects (including myocardial infarction and heart failure) and more cardiovascular deaths than other equally effective NSAIDs (*Prescrire Int* n° 167, 210, 263; *Rev Prescrire* n° 362, 374).

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• **Cox-2 inhibitors** (coxibs), i.e. ***celecoxib***, ***etoricoxib*** and ***parecoxib***, have been linked to an excess of cardiovascular events (including myocardial infarction and thrombosis) and skin reactions compared with other equally effective NSAIDs (*Prescrire Int* n° 167; *Rev Prescrire* n° 344, 361, 374, 409).
• ***Ketoprofen* gel** causes more photosensitivity reactions (eczema, bullous rash) than other equally effective topical NSAIDs (*Prescrire Int* n° 109, 137, 193).
• ***Meloxicam***, ***piroxicam*** and ***tenoxicam***, when used **systemically**, expose patients to an increased risk of gastrointestinal disorders and cutaneous disorders (including Stevens-Johnson syndrome and toxic epidermal necrolysis), but are no more effective than other NSAIDs (*Prescrire Int* n° 212; *Rev Prescrire* n° 321).

"Muscle relaxants". Various drugs used as muscle relaxants have no demonstrated efficacy beyond that of a placebo, but expose patients to the risk of sometimes severe adverse effects. An effective analgesic is a better option, with *paracetamol* as the first choice, keeping exposure to a minimum, or *ibuprofen* or *naproxen* as alternatives.
• ***Mephenesin***, taken orally, can cause drowsiness, nausea, vomiting, hypersensitivity reactions (including rash and anaphylactic shock), abuse and addiction; *mephenesin* ointment can provoke severe cutaneous adverse reactions, including erythema multiforme and acute generalised exanthematous pustulosis (*Prescrire Int* n° 125, 138; *Rev Prescrire* n° 414, 430).
• ***Methocarbamol*** has many adverse effects, in particular gastrointestinal and cutaneous disorders (including angioedema) (*Rev Prescrire* n° 282, 338, 468, 480).
• ***Thiocolchicoside***, which is related to *colchicine*, can cause diarrhoea, stomach pain, photodermatosis and possibly convulsions, and it is genotoxic and teratogenic (*Prescrire Int* n° 168; *Rev Prescrire* n° 282, 313, 321, 367, 400, 412).

Osteoarthritis. Some drugs authorised for their supposed effect on the process that results in osteoarthritis should be avoided because they have no demonstrated efficacy beyond that of a placebo, yet they can provoke sometimes serious adverse effects. As of early 2026, there are no drugs that are known to have a favourable harm-benefit balance in the reduction, stabilisation or prevention of joint degeneration.
• ***Chondroitin***, an acid mucopolysaccharide present in cartilage, has not been shown to improve clinical outcomes in osteoarthritis. It can provoke cutaneous disorders, gastrointestinal disorders, dizziness and, in rare cases, angioedema (*Rev Prescrire* n° 496).
• ***Diacerein*** can cause gastrointestinal disorders (including gastrointestinal bleeding and melanosis coli), angioedema and hepatitis (*Prescrire Int* n° 159; *Rev Prescrire* n° 282, 321).
• ***Glucosamine*** can provoke allergic reactions (angioedema, acute interstitial nephritis) and hepatitis (*Prescrire Int* n° 84, 137; *Rev Prescrire* n° 380).

Osteoporosis. Two drugs used in osteoporosis have an unfavourable harm-benefit balance. When non-drug measures, plus *calcium* and *vitamin D* supplementation, are insufficiently effective, *alendronic acid*, or *raloxifene* or *teriparatide* as alternatives, have a better harm-benefit balance in reducing the incidence of clinical fractures, despite their considerable limitations. There is no known satisfactory drug treatment for "bone loss".
• ***Denosumab* 60 mg** has very modest efficacy in the prevention of osteoporotic fractures and no efficacy for "bone loss" during prostate cancer (**e**). This monoclonal antibody carries a disproportionate risk of adverse effects, including back, muscle and bone pain, multiple fractures after its discontinuation, osteonecrosis, immune dysfunction, and serious infections (including endocarditis) due to its immunosuppressive effects (*Prescrire Int* n° 117, 130, 168, 198).
• ***Romosozumab*** is authorised for severe postmenopausal osteoporosis, on the basis of a trial in several thousand women that showed a slightly lower risk of clinical fractures than with *alendronic acid*. This slight gain must be weighed against a possible increase in the risk of cardiovascular events, with higher mortality among patients aged 75 years and older (*Prescrire Int* n° 223).

Miscellaneous. A number of other drugs used for specific types of pain or in rheumatology are best avoided.
• ***Capsaicin***, a red chilli pepper extract authorised in patch form for neuropathic pain, is barely more effective than placebo, but can provoke irritation, severe pain and second-degree burns (*Prescrire Int* n° 108, 180; *Rev Prescrire* n° 425, 455). *Capsaicin* remains an unreasonable choice even when systemic pain medications or local ones such as *lidocaine* medicated plasters fail to provide adequate relief.
• The combination of ***colchicine*** + ***opium powder*** + ***tiemonium***, used for example in gout attacks and acute pericarditis, has an unfavourable harm-benefit balance, because the action of *opium powder* and *tiemonium* can mask the onset of diarrhoea, which is an early sign of potentially fatal *colchicine* overdose (*Prescrire Int* n° 147, 211). A nonsteroidal anti-inflammatory drug, or a corticosteroid as an alternative, is a better option for gout attacks.

e- *A 120-mg strength denosumab product is authorised in various situations, including in patients with bone metastases from solid tumours. In this situation, denosumab is just one of several options, but its harms do not clearly outweigh its benefits (Prescrire Int n° 130).*

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• ***Quinine***, authorised for cramps, can have life-threatening adverse effects including anaphylactic reactions, haematological effects (including thrombocytopenia, haemolytic anaemia, agranulocytosis, and pancytopenia) and cardiac arrhythmias. These adverse effects are disproportionate in view of its poor efficacy (*Prescrire Int* n° 188; *Rev Prescrire* n° 337, 344). There are no drugs with a favourable harm-benefit balance for patients with cramps. Regular stretching can be beneficial (*Rev Prescrire* n° 362) (**f**).

Psychiatry
Addiction

Drugs for depression. Some drugs authorised for use in depression cause more severe adverse effects than others, without offering greater efficacy. Antidepressants generally have only modest efficacy and often take some time to work. It is better to choose one of the antidepressants with a longer history of use and an adequately documented adverse effect profile, taking into account the characteristics of the individual patient (*Rev Prescrire* n° 479, 489, 504).

• ***Agomelatine*** has no demonstrated efficacy beyond that of a placebo, but can cause hepatitis and pancreatitis, suicide and aggressive behaviour, rhabdomyolysis, and severe cutaneous adverse reactions including Stevens-Johnson syndrome (*Prescrire Int* n° 104, 136, 270; *Rev Prescrire* n° 397, 419, 432).

• ***Citalopram*** and ***escitalopram*** are "selective" serotonin reuptake inhibitor (SSRI) antidepressants that expose patients to a higher incidence of QT prolongation, torsade de pointes and sudden death than other SSRIs, as well as worse outcomes in the event of overdose (*Prescrire Int* n° 170, 174, 221; *Rev Prescrire* n° 369).

• ***Duloxetine***, ***milnacipran*** and ***venlafaxine*** are serotonin and noradrenaline (norepinephrine) reuptake inhibitors (SNRIs) that, as well as provoking the adverse effects of SSRI antidepressants, carry a risk of cardiac disorders due to their noradrenergic activity, including hypertension, tachycardia, arrhythmias, and QT prolongation. Compared with SSRIs, *venlafaxine* carries a higher risk of withdrawal symptoms following discontinuation, and a higher risk of cardiac arrest in cases of overdose (*Prescrire Int* n° 131, 170, 206, 250, 270; *Rev Prescrire* n° 338; *Interactions Médicamenteuses Prescrire*). *Duloxetine* can also cause hepatitis and hypersensitivity reactions with severe cutaneous effects, including Stevens-Johnson syndrome (*Prescrire Int* n° 85, 100, 111, 142; *Rev Prescrire* n° 489).

• ***Reboxetine*** is a noradrenaline reuptake inhibitor, with a weaker effect on serotonin reuptake. It appears to be less effective than other antidepressants, including *fluoxetine*, and causes antimuscarinic adverse effects, sexual dysfunction and loss of appetite (*Rev Prescrire* 489).

• ***Esketamine*** nasal spray is authorised for use in "treatment-resistant" depression and depression with a high risk of suicide, but its efficacy is highly uncertain. Its neuropsychiatric adverse effects are common and include dissociative symptoms. An increased risk of suicide was reported in the weeks following treatment. Addiction and misuse are likely (*Prescrire Int* n° 222, 238; *Rev Prescrire* n° 494). In both of these difficult clinical situations, it is more prudent to consider other less dangerous options, even if their efficacy is uncertain, for example: psychotherapy, sometimes with hospitalisation; increasing the dose of the antidepressant; or switching to an antidepressant from a different pharmacological class.

• ***Tianeptine***, a drug with no demonstrated efficacy beyond that of a placebo, can cause hepatitis, life-threatening skin reactions (including bullous rash) and addiction (*Prescrire Int* n° 127, 132, 264; *Rev Prescrire* n° 349).

Other psychotropic drugs. Some other psychotropic drugs with minimal or no demonstrated efficacy have disproportionate adverse effects.

• ***Dapoxetine*** is a "selective" serotonin reuptake inhibitor (SSRI) antidepressant used for sexual dissatisfaction related to premature ejaculation. Its adverse effects are disproportionate, given its very modest efficacy, and include aggressive behaviour, serotonin syndrome, and syncope (*Prescrire Int* n° 105; *Rev Prescrire* n° 355). A psychological and behavioural approach, or application of the anaesthetic combination of *lidocaine + prilocaine* on the glans penis are better options in this situation (*Prescrire Int* n° 197).

• ***Etifoxine*** has no demonstrated efficacy against anxiety beyond that of a placebo, but it can cause hepatitis and severe hypersensitivity reactions, including drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome and toxic epidermal necrolysis (*Prescrire Int* n° 136, 242; *Rev Prescrire* n° 349, 376, 445, 458). When an anxiolytic drug is justified, a benzodiazepine, used for the shortest possible duration, is a better choice. It is advisable to discuss with the patient when and how the drug will be discontinued from the outset, in order to reduce the risks associated with prolonged use.

Pulmonology
ENT

Cough. Although cough is sometimes very bothersome, it is generally a minor ailment. Various drugs used to relieve cough have disproportionate adverse effects given their limited efficacy. When drug therapy for cough seems justified, the opioid *dextromethorphan* is an option, despite its limitations (*Rev Prescrire* n° 358, 391). For refractory or unexplained chronic cough, in the absence of a better alternative, it is prudent to focus on reviewing the cause of the cough and on optimising non-pharmacological measures.

f- *Quinine is sometimes useful for certain patients with malaria (Prescrire Int n° 145).*

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• ***Ambroxol*** and ***bromhexine*** are mucolytics authorised for cough and sore throat. They have no demonstrated efficacy beyond that of a placebo, but they carry a risk of anaphylactic reactions and serious, sometimes fatal, cutaneous reactions such as erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis (*Prescrire Int* n° 159, 184, 192; *Rev Prescrire* n° 462).
• ***Gefapixant***, an antagonist of the purinergic receptors P2X3 and P2X2/3, authorised for refractory or unexplained chronic cough, has uncertain, and at best modest efficacy in these situations. It carries a risk of very frequent taste disturbance, as well as respiratory tract infections, in particular pneumonia, and urolithiasis (*Prescrire Int* n° 275).
• ***Oxomemazine*** is a sedating antihistamine of the phenothiazine class with antimuscarinic activity and neuroleptic properties. Its adverse effects are disproportionate for a drug used to relieve cough symptoms (*Rev Prescrire* n° 334, 386, 462; *Interactions Médicamenteuses Prescrire*).
• ***Pentoxyverine***, a centrally-acting cough suppressant, can cause cardiac disorders including QT prolongation, and serious allergic reactions (*Prescrire Int* n° 208; *Rev Prescrire* n° 462).

Sore throat. When a drug appears necessary to relieve sore throat, in conjunction with non-drug measures such as sipping water or sucking on candy, the best option is *paracetamol*, keeping exposure to a minimum.
• ***Alpha-amylase***, an enzyme with no demonstrated efficacy against sore throat beyond that of a placebo, can cause sometimes severe cutaneous or allergic disorders, including urticaria, pruritus, angioedema, maculopapular rash and erythema (*Rev Prescrire* n° 426).

Miscellaneous. A variety of other drugs used in pulmonary or ENT disorders are best avoided.
• The oral or nasal decongestants ***ephedrine***, ***naphazoline***, ***oxymetazoline***, ***pseudoephedrine*** and ***tuaminoheptane***, as well as ***phenylephrine*** and ***xylometazoline***, are sympathomimetic vasoconstrictors (**g**). They can cause serious and even life-threatening cardiovascular disorders (hypertensive crisis, stroke, and arrhythmias, including atrial fibrillation), as well as ischaemic colitis and ischaemic optic neuropathy. "Posterior reversible encephalopathy syndrome" (PRES) and "reversible cerebral vasoconstriction syndrome" (RCVS) have also been reported with *pseudoephedrine*. These adverse effects are disproportionate for drugs intended to relieve minor, rapidly self-resolving symptoms such as those associated with the common cold (*Prescrire Int* n° 136, 172, 178, 183, 208, 231, 262; *Rev Prescrire* n° 312, 342, 345, 348, 361, 424).
• ***Mannitol*** **inhalation powder**, authorised as a mucolytic for patients with cystic fibrosis despite the lack of convincing evidence of efficacy, can cause bronchospasm and haemoptysis (*Prescrire Int* n° 148). It is best to choose other mucolytics such as *dornase alfa*, in the absence of a better alternative.
• ***Nintedanib***, a tyrosine kinase inhibitor with anti-angiogenic activity, has not been shown to improve clinical outcomes in any of its authorised indications: various types of pulmonary fibrosis, and systemic sclerosis-associated interstitial lung disease. It can provoke liver injury and many severe adverse effects related to its inhibitory effect on angiogenesis, including venous thromboembolism, bleeding, hypertension, gastrointestinal perforation and impaired wound healing (*Prescrire Int* n° 173, 231, 237). It is better to focus on symptomatic treatments, despite their limitations.
• ***Roflumilast***, a phosphodiesterase-4 inhibitor with anti-inflammatory effects, has not been shown to reduce mortality or improve quality of life in patients with severe chronic obstructive pulmonary disease (COPD). It can provoke gastrointestinal adverse effects, weight loss, psychiatric disorders (including depression and suicide), and possibly cancer (*Prescrire Int* n° 134, 176). Despite its limitations, treatment for these patients is based on inhaled bronchodilators, sometimes with an inhaled corticosteroid, and possibly *oxygen* therapy.

Smoking cessation

• ***Bupropion***, a substance that is chemically related to certain amphetamines, is authorised for smoking cessation. It is no more effective than *nicotine*, but can cause neuropsychiatric disorders (including aggressiveness, depression and suicidal thoughts), potentially severe allergic reactions (including angioedema and Stevens-Johnson syndrome), addiction, and congenital heart defects in children exposed to the drug in utero (*Prescrire Int* n° 126, 131; *Rev Prescrire* n° 221, 377). When a drug is needed to help with smoking cessation, *nicotine* is a better choice, despite its limitations.

Urology

• **Oral** ***pentosan polysulfate***, a heparin derivative authorised for bladder pain syndrome (interstitial cystitis), has uncertain efficacy in relieving the symptoms of this condition, and it has serious adverse effects, including pigmentary maculopathy with visual disturbances, and immune-mediated thrombocytopenia with a consequent risk of arterial thrombosis (*Prescrire Int* n° 204, 260; *Rev Prescrire* n° 443). In the absence of a better alternative, it is more prudent to offer these patients analgesic medication and non-drug measures with a low risk of adverse effects, such as applying heat or cold to the bladder or perineum, and avoiding foods or activities that exacerbate symptoms.

g- *Phenylephrine for ocular use is sometimes an option as a mydriatic (Rev Prescrire n° 387).*

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Putting patients first

Our analysis shows that the harm-benefit balance of the drugs listed above is unfavourable in all their authorised indications (apart from a few exceptions, explained in a footnote). Yet some of these drugs have been marketed for many years and are in common use. From the patients' perspective, what possible justification is there for exposing them to a drug that has more adverse effects than other drugs belonging to the same pharmacological class, or other similarly effective drugs? And how can one justify exposing patients to a drug with severe adverse effects, when it has not been shown to be more effective than a placebo, or to improve patient-relevant clinical outcomes?

Healthcare professionals need to actively remove these drugs, which pharmaceutical companies persist in marketing, from their list of useful treatments. But regulators and health authorities must also take concrete steps to protect patients and promote the use of treatments that have an acceptable harm-benefit balance.

There is no valid reason why drugs that are more dangerous than beneficial should retain their marketing authorisations and remain on the market.

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Further reading

1- Prescrire Editorial Staff "Towards better patient care: drugs to avoid in 2025" Prescrire Int 2025; **34** (267): 52-55.

2- Prescrire Editorial Staff "Towards better patient care: drugs to avoid in 2013" Prescrire Int 2013; **22** (137): 108-111.

3- Prescrire Rédaction "Des médicaments à écarter pour mieux soigner: pourquoi?" Rev Prescrire 2013; **33** (360): 792-795.

4- Prescrire Editorial Staff "Determining the harm-benefit balance of an intervention: for each patient" Prescrire Int 2014; **23** (154): 274-277.

5- Prescrire Editorial Staff "Treatment goals: discuss them with the patient" Prescrire Int 2012; **21** (132): 276-278.

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