

numerous adverse effects, including cutaneous, haematological and renal disorders (*Prescrire Int* n° 85, 117). When a fibrate is justified, *gemfibrozil* is the only one that has been shown to prevent cardiovascular complications of hypercholesterolaemia, although renal function and serum creatine phosphokinase levels must be closely monitored.

- **Ivabradine**, an inhibitor of the cardiac I_f current, can cause visual disturbances, cardiovascular disorders (including myocardial infarction), potentially severe bradycardia and other cardiac arrhythmias. It has no advantages in angina or heart failure (*Prescrire Int* n° 88, 110, 118, 155, 165). Established treatments shown to be effective in angina include beta-blockers and the calcium channel blockers *amlodipine* and *verapamil*. There are also better options for heart failure: one is to refrain from adding another drug to an optimised treatment regimen; another is to use a beta-blocker with a proven impact on mortality.

- **Nicorandil**, a vasodilator with solely symptomatic efficacy in the prevention of effort angina, can cause severe mucocutaneous ulceration (*Prescrire Int* n° 81, 95, 110, 132). A nitrate is a better option to prevent angina attacks.

- **Olmesartan**, an angiotensin II receptor blocker (ARB or sartan) that is no more effective than other ARBs in hypertension, can cause sprue-like enteropathy with chronic diarrhoea (potentially severe) and weight loss, and, possibly, an increased risk of cardiovascular mortality (*Prescrire Int* n° 148). It is better to choose another of the many available ARBs, such as *losartan* or *valsartan*, which do not appear to have these adverse effects

- **Trimetazidine**, a drug with uncertain properties, is used in angina despite its only modest symptomatic efficacy (shown mainly in stress tests), yet it can cause parkinsonism, hallucinations and thrombocytopenia (*Prescrire Int* n° 84, 100, 106). It is better to choose better-known treatments for angina, such as certain beta-blockers or the calcium-channel blockers *amlodipine* and *verapamil*.

Dermatology - Allergy

- **Mequitazine**, a sedating antihistamine with antimuscarinic properties, used in allergies, has only modest efficacy but carries a higher risk than other antihistamines of cardiac arrhythmias due to QT prolongation in patients who are slow cytochrome isoenzyme P450 CYP2D6 metabolisers, and during

Notable changes in the 2016 update: citalopram, escitalopram, diclofenac added to the list of drugs to avoid

Three of the drugs that have featured in our list of drugs to avoid since the first version, published in 2013, were withdrawn from the French market in 2015 by the pharmaceutical companies concerned: *asenapine* for manic episodes; *iron dextran* for anaemia; and *floctafenine* for moderate pain.

Pirfenidone: not listed in 2016, but many uncertainties. All the drugs listed in our 2015 review are also included this year, with the exception of *pirfenidone*, whose harm-benefit balance in idiopathic pulmonary fibrosis has become more uncertain in light of new clinical data. Its clinical evaluation includes some favourable data but still does not show whether or not *pirfenidone* reduces mortality, even after one year. It is not clear whether the uncertain benefit of this treatment outweighs its harms, which markedly reduce the quality of life of patients whose life expectancy is short, but this does not justify its continued inclusion in our list of drugs to avoid (*Rev Prescrire* n° 384).

Confirmation: thiocolchicoside, venlafaxine, omalizumab. In 2015, we re-examined certain aspects of the harm-benefit balance of several drugs from our list of drugs to avoid. Our re-evaluation of *thiocolchicoside*, a drug with a similar chemical structure to *colchicine*, confirmed its place on the list. *Thiocolchicoside* has a variety of serious hepatic, pancreatic, muscular, haematological and neurological adverse effects, yet has not been shown to be more effective than placebo in muscle pain (*Prescrire Int* n° 168).

Re-analysis also confirmed *venlafaxine* as an antidepressant to be avoided. This antidepressant with serotonergic and noradrenergic activity causes more cardiovascular adverse effects, and is more likely to result in death in the event of overdose,

than many other antidepressants over which it has no proven advantages (*Rev Prescrire* n° 386 and *Prescrire Int* n° 170).

Omalizumab, which is authorised for use in asthma and chronic spontaneous urticaria, is no more effective than a corticosteroid. In addition to its immunosuppressant effect, this monoclonal antibody causes hypersensitivity reactions and cardiac disorders (*Prescrire Int* n° 115, 161).

Additions: drugs that are more harmful than similar options. An analysis of the cardiac adverse effects of antidepressants revealed that the "selective" serotonin reuptake inhibitors (SSRIs) *citalopram* and *escitalopram* are no more effective than other SSRIs but cause more cardiac disorders, including dose-dependent prolongation of the QT interval and torsades de pointes (*Rev Prescrire* n° 386).

Analysis of the cardiovascular adverse effects of nonsteroidal anti-inflammatory drugs (NSAIDs) revealed that *diclofenac* causes more cardiovascular adverse effects, including myocardial infarction, heart failure and cardiovascular deaths than other NSAIDs, such as *ibuprofen* (up to a maximum dose of 1200 mg per day) or *naproxen*, but is no more effective. In the absence of evidence to the contrary, *aceclofenac* was considered to expose patients to similar risks to *diclofenac* due to their chemical affiliation, and should therefore also be avoided (*Prescrire Int* n° 167; *Rev Prescrire* n° 374).

The efficacy of *defibrotide*, an antithrombotic authorised in severe hepatic veno-occlusive disease following haemopoietic stem cell transplantation, is too uncertain when balanced against its serious adverse effects, in particular haemorrhages (*Prescrire Int* n° 164).

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co-administration of drugs that inhibit this isoenzyme (*Rev Prescrire* n° 337). A non-sedating antihistamine without antimuscarinic activity, such as *loratadine* or *cetirizine*, is a better option in this situation.

- **Omalizumab** in chronic spontaneous urticaria (see the Pulmonology - ENT section on p. 111) (*Prescrire Int* n° 161).
- Injectible **promethazine**, an antihistamine used to treat severe urticaria, can cause thrombosis, skin necrosis and gangrene following extravasation or

inadvertent injection into an artery (*Rev Prescrire* n° 327). Injectible *dexchlorpheniramine*, which does not appear to carry these risks, is a better option.

- Topical **tacrolimus**, an immunosuppressant used in atopic eczema, can cause skin cancer and lymphoma, yet its efficacy is barely different from that of topical corticosteroids (*Prescrire Int* n° 101, 110, 131; *Rev Prescrire* n° 367). Judicious use of a topical corticosteroid to treat flare-ups is a better option in this situation. ►►