Drugs best avoided yet still on the market in early 2012

Many drugs that have more harms than benefits are still marketed in France, and in some cases, for several decades. The following drugs were examined in Prescrire in 2011, in order of publication:

- nimesulide, a nonsteroidal anti-inflammatory drug (NSAID), because of the risk of liver damage (Prescrire Int n° 116);
- angiotensin antitussives, because of their sedative and antimuscarinic effects (issue 329 p. 179);
- drenoralone, an antiarrhythmic drug, due to a risk of liver damage and cardiovascular disorders (Prescrire Int n° 122);
- terpenes, due to their neuropsychiatric adverse effects (including seizures), especially in young children. In 2011, some medicines for children, mainly suppositories, still contained terpenes. In late 2011, the French drug regulatory agency contraindicated their use in suppositories for children under 30 months (Prescrire n° 340);
- trimetazidine, marketed for angina, dizziness, visual disorders and tinnitus, carries a risk of extrapyramidal disorders, falls and thrombocytopenia (Prescrire Int n° 115). In 2011, the French regulatory agency triggered a referral to the European Medicines Agency;
- pholcodine, an opioid antitussive, because of concerns over a risk of allergy to muscle relaxants used during anaesthesia (Prescrire n° 331). In 2011, the French agency simply ruled that this drug should be available by prescription only, in order to limit its use (Prescrire n° 333);
- oral and nasal vasoconstrictive decongestants (ephedrine, naphazoline, oxymetazoline, phenylephrine, pseudoephedrine and tramcinolone), because of a risk of life-threatening cardiovascular disorders (myocardial infarction, arrhythmia, hypertension). In 2011, the French agency simply demanded a modification in the Summary of Products Characteristics (SPC) (Prescrire n° 335);
- iron dextran, due to a higher risk of hypersensitivity than with iron sucrose (Prescrire n° 335);
- meprobamate is still contained in certain products in France (for gastrointestinal disorders associated with anxiety, and premenstrual syndrome), despite a risk of severe cutaneous and haematological adverse reactions, and a withdrawal syndrome (Prescrire Int n° 123);
- bupropion, an amphetamine derivative, and varenicline, an acetylcholine receptor partial agonist used for smoking cessation, mainly because of cardiovascular and neuropsychiatric disorders (Prescrire n° 329, Prescrire Int n° 124);
- quinine for cramps, because of a risk of haematological disorders, cardiac arrhythmia and hypersensitivity (Prescrire Int n° 115);
- mequitazine, a “sedative” and “atropinic” antihistamine used in allergies, carries a higher risk of cardiac arrhythmia than other antihistamines. In 2011, the French agency simply placed mequitazine on the list of controlled substances (Prescrire n° 337);
- ropinirole, a dopamine agonist used for restless legs syndrome (Prescrire Int n° 115);
- orlistat for weight loss: its adverse effects and interactions largely outweigh a marginal and transient weight loss (Prescrire n° 338);

Since late 2011, some of these products are no longer reimbursed in France, including those based on drenoralone, nimesulide and quinine (for cramps). While the measures limit the consumption of these drugs and, thus, the number of patients exposed, they send a mixed message to patients. Simply withdrawing them from the market is the most effective solution.

Orphan drugs: in decline. According to European regulations, “orphan” drug status is granted by the European Commission for medications aimed at treating patients with rare diseases, based on the opinion of the European Medicines Agency (EMA). Drug companies that develop and market such products enjoy certain advantages, including market exclusivity. None of the 6 orphan drugs examined by Prescrire in 2011 represented a real breakthrough.

Generic drugs with uneven therapeutic value. In 2011, Prescrire examined the harm-benefit balance of 27 generic drugs marketed in France.

Ten of these drugs are useful in certain situations: intradural baclofen for some cases of severe chronic spasticity (Prescrire n° 332); clobetasol, a potent topical corticosteroid for some skin conditions (Prescrire n° 328); dacarbazine for some cancers (Prescrire n° 330); eprostenol for pulmonary arterial hypertension (Prescrire n° 328); letrozole in breast cancer (Prescrire n° 333); levetiracetam for various forms of epilepsy (Prescrire n° 336); mefloquine (Prescrire n° 337) and teicoplanin in severe infections (Prescrire n° 331), modafinil for narcolepsy (Prescrire n° 329); and valsartan (with or without hydrochlorothiazide) for hypertension, heart failure and recent myocardial infarction (Prescrire n° 336).

Many other generic drugs are best avoided, including milnacipran in severe depression (Prescrire n° 338), niacinamide in angina pectoris (Prescrire n° 33), and rivastigmine in Alzheimer’s disease and in dementia associated with Parkinson’s disease (Prescrire n° 337).

Marketing applications for generic drugs give regulatory agencies an opportunity to reassess the value of the originator drugs, and to withdraw those with a negative harm-benefit balance. Apparently they are not taking advantage of this opportunity.

Patient protection

In 2011, the French health authorities finally started to react, by protecting patients from several drugs that have more harms than benefits (see page 110).

Market withdrawals: the most effective measure, often taken late. Drug reassessment can result in measures that support patients’ interests, such as market withdrawal of drugs with a negative harm-benefit balance.

In 2011, the French drug regulatory agency finally started to withdraw some of these products, many of which had been on the market for decades:

- buflomedil, a vasodilator marketed for over 30 years (Prescrire n° 327, n° 329);
- the fixed-dose combination of dorzolamide + acetazolamide + acetazolamide, available for nearly 40 years in insomnia (Prescrire n° 335);
- oral ketoconazole, an antifungal drug that can cause severe liver damage (Prescrire n° 335);