Lamotrigine: cardiac arrhythmias

In March 2021, the US drug regulatory agency (FDA) issued a safety announcement following reports of cardiac disorders in patients taking *lamotrigine*, an antiepileptic drug also used as a "mood stabiliser". These disorders consisted of chest pain, syncope, cardiac arrest and electrocardiographic abnormalities (1).

In vitro studies have shown that *lamotrigine* exhibits class 1B antiarrhythmic activity at therapeutic plasma concentrations. It slows ventricular conduction, with widening of the QRS complex on the electrocardiogram, via a mechanism linked to inhibition of sodium channels. The US prescribing information for proprietary drugs based on *lamotrigine* has been modified to include a proarrhythmic effect, which carries a risk of sudden death, especially in patients with pre-existing heart disease (1).

In France, as of mid-2021, the SPC only mentions the electrocardiographic changes, with widening of the QRS complex, in cases of overdose (2-5). It does not mention cardiac adverse effects at therapeutic doses, other than in patients with Brugada syndrome, a genetic disease leading to ventricular arrhythmias (2-5).

A risk of cardiac arrhythmias is plausible with other sodium channel inhibitors, used mainly in epilepsy, such as *carbamazepine*, *eslicarbazepine* and *oxcarbazepine*, *phenytoin* and *fosphenytoin*, *lacosamide*, *rufinamide*, *topiramate* and *zonisamide* (1). The French SPC for the proprietary drug Tegretol®, based on *carbamazepine*, lists, as cardiac adverse effects, conduction disorders, arrhythmias, atrioventricular block with or without syncope, bradycardia and tachycardia. It also specifies a contraindication in the presence of atrioventricular block (6).

IN PRACTICE The risk of cardiac arrhythmias, including sudden death, must be weighed against the benefits expected from *lamotrigine* for each patient, particularly in the presence of heart disease. An abnormal heart rhythm, palpitations, shortness of breath, dizziness or syncope are warning signs.

► Translated from *Rev Prescrire* October 2021 Volume 41 N° 456 • Page 750

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Biotin: interference with laboratory tests

In February 2021, the United States consumer advocacy organisation Public Citizen issued a reminder regarding interference between biotin (vitamin H or B8) and laboratory tests (1).

Many laboratory analyses use biotin because of its ability to bind to a large number of substances. If biotin is present in large quantities in plasma samples, it is liable to interfere with these tests. The tests affected are mainly those performed for: diagnosis and follow-up of cardiovascular, endocrine (especially thyroid), neoplastic and infectious diseases; identification of the causes of anaemia or infertility; and investigation of disorders of bone metabolism or an inflammatory syndrome. For example, in one patient who was taking biotin, a falsely low cardiac troponin assay result led to failure to diagnose a myocardial infarction, which was fatal. Various tests used in histopathology can also be rendered inaccurate (1,2).

Biotin is a vitamin widely found in food and produced by the intestinal flora. Biotin deficiency is very rare, other than in inherited biotinidase deficiency or prolonged parenteral nutrition (3). It manifests as skin disorders, hair loss, conjunctivitis, ataxia and developmental delay in children (3,4). The recommended daily intake of biotin for adults is 0.03 mg according to the US Food and Drug Administration (FDA) and 0.04 mg according to the French Agency for Food, Environmental and Occupational Health and Safety (ANSES) (4,5). Biotin is marketed with the status of a drug or a food supplement, sometimes at doses hundreds of times higher than the recommended daily intake (6).

IN PRACTICE When a blood test is to be carried out, it is advisable to discuss with the patient the risk of an erroneous result linked to taking biotin, and to notify the testing laboratory where necessary.

► Translated from *Rev Prescrire* August 2021 Volume 41 N° 454 • Page 585

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