Temsirilimus: risk of myocardial infarction

Since 2016, the EU summary of product characteristics (SPC) for Torisel®, which contains the cytotoxic immunosuppressant temsirolimus, states that “the known association of temsirolimus with hyperlipaemia may predispose to myocardial infarction” (1,2). This information was added following the European Pharmacovigilance Risk Assessment Committee’s (PRAC) analysis of 17 cases of myocardial infarction, 3 of which were fatal, that occurred between 1 day and 9 months after starting temsirolimus therapy. In 8 cases, temsirolimus was the only drug suspected (3,4). Temsirolimus is known to provoke hyperlipaemia, hypercholesterolaemia and hypertension (1,2).

In the European Union, temsirolimus is authorised for use in metastatic renal cell carcinoma and mantle cell lymphoma. After intravenous administration, it is rapidly metabolised to sirolimus, another immunosuppressant, which is authorised for the prevention of organ rejection in certain transplant recipients (1,2,5).

In practice The risk of myocardial infarction is another addition to temsirolimus’s already long list of adverse effects (1,2). As of 7 June 2017, this risk is not mentioned in either the EU SPC or patient leaflet for sirolimus, despite adverse effects that are largely shared by temsirolimus and sirolimus (5,6).

Pholcodine: anaphylactic reactions to neuromuscular blockers

Pholcodine, an opioid used as a cough suppressant for decades, appears to be implicated in the occurrence of sometimes fatal anaphylactic shock during anesthesia as a result of cross-reactivity to neuromuscular blocking agents, such as suxamethonium (1).

In Norway, pholcodine was withdrawn from the market in 2007, and within 3 years the number of anaphylactic reactions to neuromuscular blockers had decreased (1).

In late 2016, six years after market withdrawal of pholcodine, a Norwegian team published a follow-up study (2). The frequency of anaphylactic reactions to neuromuscular blocking agents has decreased by about one-third since 2007. No deaths resulting from anaphylactic reactions to neuromuscular blockers were recorded during the last 3-year period studied, versus 5 deaths during the first 3 years when pholcodine was on the market. The prevalence of anti-suxamethonium antibodies in 300 serum samples from so-called allergic patients dropped to zero percent in 2012.

The situation in Norway seems to be approaching that of Sweden, where the last syrup containing pholcodine was withdrawn from the market at the end of the 1980s. Anaphylactic reactions to neuromuscular blockers are now very rare, with one case reported every 1 or 2 years. In Denmark, pholcodine has never been available, and anaphylactic reactions to neuromuscular blockers are extremely rare (2).

In practice Pholcodine is still available in many cough suppressants. Despite the known harms of a drug that is not useful, health authorities and pharmaceutical companies have not taken a decision to withdraw pholcodine from the market in order to protect patients. Faced with this dangerous inertia, it is up to healthcare professionals to protect patients by routinely avoiding the use of pholcodine and offering better solutions.