Temsirolimus: 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).

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1- Prescrire Editorial Staff "Temsirolimus. Metastatic kidney cancer: more assessment needed" *Prescrire Int* 2008; **17** (98): 223-225.
2- European Commission "SPC + package leaflet + annex IV-Torisel" 14 January 2016 + "SPC-Torisel" 15 October 2015: 69 pages.
3- EMA - PRAC "Minutes of the meeting on 07-10 April 2015" 7 May 2015: 78 pages.
4- Boyd Y "Temsirolimus and myocardial infarction" WHO Pharmaceuticals Newsletter 2015; 1: 29-33.
5- EMA "SPC + package leaflet-Rapamune" 21 July 2016: 103 pages.
6- Prescrire Rédaction "10-1. Patients greffés" *Rev Prescrire* 2015; **35** (386 suppl. Interactions Médicamenteuses).

Pholcodine: anaphylactic reactions to neuromuscular blockers

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In Norway, *pholcodine* was withdrawn from the market in 2007, and within 3 years the number of anaphylactic reactions to neuromuscular blockers had decreased (1).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

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1- Prescrire Rédaction "Pholcodine: anaphylaxie aux curares" *Rev Prescrire* 2011; **31** (331): p.349.
2- De Pater GH "Six years without pholcodine; Norwegians are significantly less IgE-sensitized and clinically more tolerant to neuromuscular blocking agents" *Allergy* 2016: 20 pages.

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