**Adverse Effects**

Transcribed from *Rev Prescrire* July 2013; 33 (357): 512

**Strontium: myocardial infarction**

- This adds to an already burden-some adverse effect profile. Do not use strontium.

According to the European Medicines Agency (EMA), the results of a meta-analy-sis of clinical trials of strontium ranelate in 7500 postmenopausal women with osteoporosis showed a statistically significant increase in the risk of myocardial infarction in the groups that received strontium ranelate: 1.7% versus 1.1% in the placebo groups (1).

An increased incidence of cardiovascular deaths had already been reported in 2004, in the scientific discussion of the initial EMA assessment report on strontium ranelate (2). Strontium ranelate exposes patients to a risk of other serious adverse effects, including venous throm-bosis and embolism, multiorgan hypersensitivity syndrome, and serious skin disorders, including toxic epidermal necrolysis (Lyell’s syndrome) (3).

The efficacy of strontium ranelate in reducing the risk of symptomatic fractures has not been demonstrated. Therefore, exposing patients to the risk of all of these serious adverse effects is not acceptable. Its unfavourable harm-benefit balance has been known for several years. How many more victims will there be before it is withdrawn from the market?

**Selected references from Prescrire’s literature search.**

1- EMA “Recommendation to restrict the use of Protelos/Oseeor (strontium ranelate) CHMP confirms recommendation from the PEAC” 23 April 2013: 3 pages.

Transcribed from *Rev Prescrire* July 2013; 33 (357): 512

**Goji berries and anticoagulants: bleeding**

- Informing patients is key.

Goji berries are known as wolfberries, are used in traditional Chinese medicine (1). Various beneficial properties have been attributed to them. Goji berries expose patients taking vitamin K antagonists to the risk of bleeding. A few reports of bleeds and INR elevations have been published, including 4 cases reported in Germany (2,3). The mechanism underlying this interaction is unknown; cytochrome P450 inhibition has been postulated (1). According to the independent German pharmacovigilance centre Arznei-Telegramm, drinking three or four cups of goji tea daily or 30 ml of goji juice twice daily can increase INR levels and result in bleeding (1).

This example serves as yet another reminder that patients taking a vitamin K antagonist must be informed that certain plants used as herbal remedies can interfere with its anticoagulant effect.

**Selected references from Prescrire’s literature search.**

2- Rivera CA et al. “Probable interaction between Lycium barbarum (Goji) and warfarin” Pharma-cotherapy 2012; 32 (3): e50-e53.

**Terbinafine: taste and smell disorders**

- Sometimes long-lasting.

In early 2013, the Dutch pharmacovigilance centre Lareb published a report on 15 cases of smell disorders attributed to terbinafine that are contained in its database (1). Eight patients had a taste disorder in addition to the smell dis-order. These disorders developed one day to several weeks or even several months after exposure to terbinafine and in some cases, they did not resolve after terbinafine discontinuation.

Taste disturbance is a known adverse effect of terbinafine (2). Depending on the source, it has been estimated to occur in 0.6% to 2% of patients exposed to this drug (1,3). According to the US summa-ry of product characteristics, these taste and smell disorders are sometimes pro-longed or even permanent (3). The under-lying mechanism is unknown (1).

In patients with superficial fungal infec-tion, topical treatment is usually effect-ive (3). Oral terbinafine is known to expose patients to the risk of sometimes serious adverse effects, such as skin reactions, hepatotoxicity or haematolog-ical disorders, and disabling conditions such as loss of taste or smell.

When terbinafine is nonetheless used, patients should be properly informed of the potential harms and advised to dis-continue the drug if necessary.

**Selected references from Prescrire’s literature search.**

2- Rivara CA et al. “Probable interaction between Lycium barbarum (Goji) and warfarin” Pharma-cotherapy 2012; 32 (3): e50-e53.

**SSRI antidepressants: brain haemorrhage**

- Assess risk of serious bleeding before use.

So-called selective serotonin reuptake inhibitor (SSRI) anti-depressants can cause bleeding, particularly in the gastrointestinal tract (1). The mechanism is thought to be mediated by serotonin, which is involved in platelet aggregation (2).

A meta-analysis of 16 epidemiological studies of brain haemorrhage was pub-lished in late 2012. Patients in the SSRI groups were more likely to experience intracranial haemorrhage than those in the control groups: estimated relative risk of 1.5 (95% confidence interval (95CI): 1.3 to 1.8). The increased risk seemed to con-cern intracerebral haemorrhage, but not subarachnoid haemorrhage. Concomi-tant treatment with an SSRI antidepres-sant and a vitamin K antagonist resulted in an increased risk of bleeding com-pared to treatment with a vitamin K antag-onist alone (RR = 1.6, 95CI: 1.3 to 1.8).

In practice, this risk should be taken into account, especially in patients who already have bleeding disorders or a his-tory of intracranial haemorrhage, or who are taking drugs known to increase the risk of bleeding.

**Selected references from Prescrire’s literature search.**