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Strontium: myocardial infarction

● **This adds to an already burdensome adverse effect profile. Do not use strontium.**

According to the European Medicines Agency (EMA), the results of a meta-analysis 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 thrombosis 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 How many more victims will there be before it is withdrawn from the market?

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Selected references from Prescrire's literature search.
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Goji berries and anticoagulants: bleeding

● **Informing patients is key.**

Goji berries (*Lycium barbarum*), also 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.

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Selected references from Prescrire's literature search.
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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 disorder. 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 summary of product characteristics, these taste and smell disorders are sometimes prolonged or even permanent (3). The underlying mechanism is unknown (1).

In patients with superficial fungal infection, topical treatment is usually effective (3). Oral *terbinafine* is known to expose patients to the risk of sometimes serious adverse effects, such as skin reactions, hepatotoxicity or haematological 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 discontinue the drug if necessary.

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SSRI antidepressants: brain haemorrhage

● **Assess risk of serious bleeding before use.**

So-called selective serotonin reuptake inhibitor (SSRI) antidepressants 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 published 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 concern intracerebral haemorrhage, but not subarachnoid haemorrhage. Concomitant treatment with an SSRI antidepressant and a vitamin K antagonist resulted in an increased risk of bleeding compared to treatment with a vitamin K antagonist 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 history of intracranial haemorrhage, or who are taking drugs known to increase the risk of bleeding.

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