**New indication**

strontium ranelate for osteoporosis in men

**More dangerous than beneficial**

- Increasingly numerous and potentially serious adverse effects have been reported since market release. There was no preventive effect on symptomatic fractures in a trial with 261 men.

Osteoporotic fractures are less frequent in men than in women but their consequences are often more severe (1). Prevention of these fractures is based mainly on measures designed to reduce the risk of falls, together with controlled intake of calcium and vitamin D, sunlight exposure, and exercise.

There is little evidence to support drug therapy for osteoporosis in men, and current drugs have not been shown to prevent symptomatic fractures (1,2).

Strontium is a cation with properties similar to those of calcium. Strontium ranelate (Protelos®, Servier) has a negative harm-benefit balance in postmenopausal osteoporosis: serious and even life-threatening adverse effects have been reported since market release in 2005 (3-5). Yet strontium ranelate is now also licensed for the treatment of osteoporosis in men. So does it prevent symptomatic fractures in men, and are there other adverse effects?

No proven efficacy. Clinical evaluation of strontium ranelate in men is mainly based on a double-blind, randomised, placebo-controlled trial, in which all patients also received calcium and vitamin D (6). The study population included 261 men with an average age of 73 years and low bone mineral density due to causes other than metabolic disorders and drugs. 28% of the men had a history of vertebral fracture and 11% a history of peripheral osteoporotic fracture (6).

This trial was not designed to assess the frequency of symptomatic fractures but simply the change in bone mineral density after 1 year of treatment with strontium ranelate. This endpoint is a poor surrogate for the risk of fractures (1,6).

After 2 years of treatment the incidence of symptomatic non-vertebral fractures, recorded as adverse effects, was about 4% in both groups (6).

Disproportionate risks. This small trial did not modify the already known safety profile of strontium ranelate (6). Indeed, this drug’s adverse effects are numerous and can be fatal: they include gastrointestinal disorders; muscle damage; neuropsychiatric disorders (especially in the elderly and patients with renal impairment); deep vein thrombosis and pulmonary embolism; and hypersensitivity reactions such as Lyell’s syndrome and DRESS (drug reactions with eosinophilia and systemic symptoms) (2-5).

In 2012, information on a risk of pulmonary embolism was added to the Contraindications section of the European summary of product characteristics (SPC) for strontium ranelate, while a risk of serious cutaneous reactions was added to the Warnings section. In late 2012 the European SPC also mentioned a risk of paraesthesia, dry mouth, dizziness and malaise which have been observed after market release (7).

In practice: do not use. Prevention of osteoporotic fractures in men should focus on non-drug measures, along with calcium and vitamin D supplementation if necessary. Strontium ranelate should be avoided because it is more dangerous than beneficial.

**strontium ranelate**

**PROTELOS**

Granules for oral suspension

• 2 g of strontium ranelate per sachet

**treatment of osteoporosis**

New indication: “Treatment of osteoporosis in adult men at increased risk of fracture”.

In response to our request for information, Servier provided us with no documentation on its product.

3- Prescrire Editorial Staff “Strontium postmenopausal osteoporosis: too many unknowns” Prescrire Int 2005; 14 (80): 207-211.
5- Prescrire Editorial Staff “Strontium ranelate: too many adverse effects” Prescrire Int 2012; 21 (125): 72.
7- EMA – CHMP “Procedural steps taken and scientific information after authorisation for Proteolos (last updated)” 07 November 2012 : 10 pages.

Selected references from Prescrire’s literature search.