

strontium ranelate for osteoporosis in men

NEW INDICATION

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.



NOT ACCEPTABLE

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.

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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".

[EU marketing authorisation, centralised procedure]

Selected references from Prescrire's literature search.

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

- 1- Prescrire Rédaction "Les fractures ostéoporotiques chez les hommes. Deux fois moins fréquentes que chez les femmes" *Rev Prescrire* 2003 ; **23** (240) : 455-459.
- 2- Prescrire Rédaction "20-2. Patients ayant une ostéoporose" *Rev Prescrire* 2012 ; **32** (350 suppl. interactions médicamenteuses).
- 3- Prescrire Editorial Staff "Strontium postmenopausal osteoporosis: too many unknowns" *Prescrire Int* 2005; **14** (80): 207-211.
- 4- Prescrire Editorial Staff "Strontium ranelate: too many adverse effects" *Prescrire Int* 2011; **20** (117): 154.
- 5- Prescrire Editorial Staff "Strontium ranelate: too many adverse effects" *Prescrire Int* 2012; **21** (125): 72.
- 6- EMA - CHMP "Type II variation assessment Report for Protelos. EMEA/H/C/560/II/31" 24 May 2012 : 59 pages.
- 7- EMA - CHMP "Procedural steps taken and scientific information after authorisation for Protelos (last updated)" 07 November 2012 : 10 pages.