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Strontium still authorised despite an unfavourable opinion of the European pharmacovigilance committee

● **In 2014 the indications of *strontium ranelate* were further restricted in the European Union, and the French pharmacoeconomic committee has finally judged strontium ranelate to have "insufficient medical benefit".**

Strontium ranelate (Protelos° - Servier), a drug authorised in the European Union for severe osteoporosis, has at best only modest efficacy in secondary prevention of vertebral fractures (1). In stark contrast, it carries a risk of disproportionate adverse effects, including myocardial infarction, embolism, vein thrombosis, hypersensitivity reactions (including Lyell's syndrome and Dress (drug reaction with eosinophilia and systemic symptoms)), impaired consciousness, seizures, hepatitis and cytopenia (1-4). Ocular disorders (loss of visual acuity and inflammation) have also been reported (5).

In early 2014, as part of a European reassessment, the European Pharmacovigilance Risk Assessment Committee (PRAC) recommended suspending marketing authorisation for products containing *strontium ranelate* in the European Union (**a**)(1).

The European Committee for Medicinal Products for Human Use (CHMP) considered that *"the cardiovascular risk in patients taking Protelos can be managed by restricting its use to patients with no history of heart and circulatory problems (…). In addition, patients (...) should be screened and monitored regularly, every 6 to 12 months"* (6,7). Ten Member States, including France, disagreed with this conclusion (7).

In April 2014, the European Commission approved the CHMP recommendation and allowed *strontium ranelate* to remain on the market (8). This decision is binding on all EU Member States. The French health products agency (ANSM) which had advised against starting treatment with *strontium ranelate* pending the European Commission's decision, had to inform healthcare professionals of the new instructions for *strontium ranelate*, which notably include last-resort use only, and regular cardiovascular monitoring (1,7). In July, the French pharmacoeconomic committee considered that *strontium ranelate* still had "insufficient medical benefit" under these new conditions (9).

Once again, the CHMP, followed by the European Commission, favours drug companies over patients' health. In practice, it is best to follow the advice of PRAC: this drug should have been discarded long ago.

a- *In early 2014 Servier withdrew an application in the European Union to extend the indications of Protelos° to osteoarthritis of the hip and knee, the CHMP having underlined the weak efficacy and uncertain long-term benefits in view of the known risk of serious adverse effects (ref 10). The company also withdrew its EU application for a fixed-dose combination of cholecalciferol + strontium ranelate in osteoporosis, the CHMP having detected problems with the manufacturing dossier (ref 11).*

Selected references from Prescrire's literature search.

1- Prescrire Rédaction "Strontium: le Comité européen de pharmacovigilance contre le maintien des AMM" *Rev Prescrire* 2014; **34** (365): 185.

2- Prescrire Rédaction "Strontium: comment justifier tous ces risques ?" *Rev Prescrire* 2013; **33** (361): 820 + 34 (365): 162.

3- Prescrire Rédaction "20-2. Patients ayant une ostéoporose" *Rev Prescrire* 2013; **33** (362 suppl. interactions médicamenteuses).

4- EMA "Protelos and Osseor. Strontium ranelate. CHMP scientific conclusions and PRAC assessment report of the review under article 20 of regulation (EC) n° 726/2004" 28 February 2014: 29 pages.

5- EMA "PRAC minutes of the meeting on 2-5 December 2013" 9 January 2014: 58 pages.

6- EMA "European medicines agency recommends that Protelos/Osseor remain available but with further restrictions" 21 February 2014: 3 pages.

7- ANSM "Point d'information - Le CHMP recommande le maintien sur le marché de Protelos (ranélate de strontium) en restreignant de nouveau ses indications" 27 February 2014 + "Lettre aux professionnels de santé - Protelos (…): nouvelles restrictions d'indication" 24 March 2014: 5 pages.

8- European Commission "Commission implementing decision (…) amending modifiant the marketing autorisation for "Protelos - strontium ranelate" (…)" + "Annexes" 15 April 2014: 46 pages.

9- HAS - Commission de la transparence "Avis de la Commission - Protelos" 9 July 2014: 23 pages.

10- EMA "Questions and answers. Withdrawal of the applications for a change to the marketing authorisation of Protelos" 23 May 2014: 2 pages.

11- EMA "Questions and answers. Withdrawal of the marketing authorisation applications for Ditelos and Issarlos" 25 April 2014: 2 pages.