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The clinical effectiveness and cost-effectiveness of strontium ranelate for the prevention of osteoporotic fragility fractures in postmenopausal women.

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OBJECTIVES: To estimate the clinical effectiveness and cost-effectiveness of strontium ranelate for the prevention of osteoporotic fractures in postmenopausal women, at different levels of absolute fracture risk. This considers secondary prevention in women who have sustained a previous fracture and primary prevention in those women without a previous fracture, as women with osteoporosis are asymptomatic until a fracture is sustained.

DATA SOURCES: Major electronic bibliographic databases were searched in September 2004 and updated in March 2005.

REVIEW METHODS: A systematic review was carried out to determine clinical effectiveness using the major electronic bibliographic databases and handsearching reference lists of relevant articles and sponsor submissions. Data from selected studies were assessed and included in the meta-analyses, if appropriate. The model used to calculate cost-effectiveness ratios was an updated version of Sheffield Health Economic Model for Osteoporosis that was populated with absolute risk of fractures using an algorithm being developed for the World Health Organization and supplied in confidence to the authors. The model calculated the number of fractures that occur and provided as output data the costs associated with osteoporotic fractures, and the quality adjusted life-years (QALYs) accrued by a cohort of 100 osteoporotic women, with each fracture being detrimental to health and incurring a cost. When the costs of the intervention were included, the incremental cost compared with no treatment was calculated and divided by the gain in QALYs to calculate cost-effectiveness measures. Treatment with strontium ranelate was calculated against a no-treatment option to evaluate whether it could be given cost-effectively. An incremental analysis against alendronate was also conducted to estimate the cost-effectiveness of strontium ranelate relative to a current standard treatment. The cost-effectiveness of strategies for identifying and treating women without a prior fracture used the risk of fracture as an input to the cost-effectiveness model.

RESULTS: Three trials were identified. Pooled data from two studies indicate that strontium ranelate therapy is associated with a reduction in the risk of vertebral fracture [relative risk (RR) compared with placebo 0.60, 95% confidence interval (CI) 0.53 to 0.69, $p < 0.001$] and non-vertebral fracture (RR 0.84, 95% CI 0.73 to 0.97, $p = 0.01$). In general,

strontium ranelate therapy did not seem to be associated with an increased risk of adverse events. However, the risk of one rare but serious adverse event, venous thromboembolism (including pulmonary embolism), was found to be significantly higher in patients receiving strontium ranelate compared with placebo (RR 1.42, 95% CI 1.02 to 1.98, p = 0.036). Some nervous system disorders, including mental impairment, disturbed consciousness, memory loss and seizures, were also more common in patients randomised to strontium ranelate. Strontium ranelate provided gains in QALYs compared with no treatment in women with sufficient calcium and vitamin D intakes. The size of the QALY gain for each intervention was strongly related to the absolute risk of fracture. From the algorithm used, it is seen that strontium ranelate can be used cost-effectively in women at relatively high risk of osteoporotic fracture. However, the results of the probabilistic sensitivity analysis, using efficacy data from randomised controlled trials, suggest that it is not as cost-effective as alendronate, a comparator intervention from the bisphosphonate class. The use of strontium ranelate in women without a prior fracture will be dependent on identification algorithms being produced in conjunction with the National Institute for Health and Clinical Excellence Osteoporosis Guidelines Development Group.

CONCLUSIONS: Strontium ranelate was shown to be **clinically effective in the prevention of osteoporotic fractures.** Scenarios have been found where strontium ranelate **can be used cost-effectively**, however given the probabilistic sensitivity analyses conducted, **this intervention appears to be less cost-effective than the bisphosphonate alendronate**. The evidence base for the efficacy of fracture prevention for strontium ranelate needs to be strengthened, particularly for hip fractures, where there is currently a non-significant reduction. If it were believed that the efficacy of strontium ranelate is dependent on either age or absolute risk, this would need to be proven. The evidence base on the T-score by age of the general female population needs to be strengthened, particularly in women over the age of 80 years. The prevalence of risk factors associated with fracture rates, over and above that provided by bone mineral density, also needs to be significantly strengthened to ensure that the estimated number of women that could be cost-effectively treated is accurate.

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