APPENDIX A

NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

Health Technology Appraisal

Final Scope

Strontium ranelate for the prevention of osteoporotic fractures in post-menopausal women with osteoporosis

Objective: To establish the clinical and cost effectiveness of strontium ranelate (Protelos, Servier Laboratories Ltd.) for the prevention of osteoporotic fractures in post-menopausal women with osteoporosis, and to provide guidance to the NHS in England and Wales[1].

Background: Osteoporosis is defined as a progressive, systemic skeletal disorder characterised by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. Osteoporotic fragility fractures occur most commonly in the vertebrae, hips and wrists, and are frequently associated with substantial disability, pain and reduced quality of life. In the absence of fracture, the condition is asymptomatic and often remains undiagnosed.

Bone mineral density (BMD) is frequently used as a proxy measure for bone strength. Two diagnostic thresholds, using BMD, have been proposed for caucasian women. The first defines women with BMD that is two and a half standard deviations (SD) or more below the young adult mean value (i.e. T score <-2.5 SD) as having osteoporosis. The second defines women with a T score that lies between -1 and -2.5 SD as having osteopenia or low bone mass. Women with BMD of <-2.5 SD and one or more fragility fractures are defined as having established osteoporosis.

While osteoporosis can occur in all populations at all ages, it is most prevalent in caucasian post-menopausal women. It is estimated that in women over the age of 50, the lifetime risk of vertebral fracture is about one in three (including asymptomatic vertebral fractures), and that for hip fracture is approximately one in six. One tenth to one fifth of women who have a hip fracture dies within the following year. An estimated 1.2 million women have osteoporosis in England and Wales. In 2000, it was estimated that the total cost of treating osteoporotic fractures in postmenopausal women was between £1.5 and £1.8 billion. This is expected to increase to £2.1 billion by 2010.

A number of interventions are used to preserve bone mass and prevent fracture. Lifestyle modifications include regular weight-bearing exercise, avoidance of smoking, and moderation of alcohol intake. In older patients, fall prevention measures, such as home modifications, and hip protectors may

also be considered. Drug therapies and supplements include hormone replacement therapy (HRT)[1], bisphosphonates, selective oestrogen receptor modulators (SERMs), parathyroid hormone, calcitonin, calcium, vitamin D, and calcitriol.

The technology: Strontium ranelate is an oral agent, which reduces the activity of osteoclasts without concomitantly reducing bone formation. Bone formation is increased by stimulation of pre-osteoblastic proliferation and by increased collagen and non-collagenic protein synthesis by mature osteoblasts. Bone resorption is reduced by inhibition of osteoclast differentiation. Strontium ranelate is not currently licensed in the UK. In June 2004, the CHMP adopted a positive opinion recommending to grant a marketing authorisation for strontium ranelate 'for the treatment of postmenopausal osteoporosis to reduce the risk of vertebral and hip fractures'.

Intervention(s)	Strontium ranelate
Population(s)	Post-menopausal women with osteoporosis who are considered to be at risk of osteoporotic fractures including those who have and have not had a previous fracture.
Current standard treatments (comparators)	• Management strategies without the use of drugs affecting bone metabolism • If the evidence allows strontium ranelate will be compared with other drugs that affect bone metabolism as follows: bisphosphonates, selective oestrogen receptor modulators, parathyroid hormone and calcitonin.
Outcomes	Outcomes to be considered include: • Osteoporotic fractures (including hip and vertebra) • Survival • Adverse effects of treatment • Health related quality of life
Economic analysis	The cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. Costs will be considered from an NHS and Personal Social Services perspective.

[1] The CSM has advised that HRT should not be considered first-line therapy for long-term prevention of osteoporosis in women over 50 years of age.

Other considerations	If the evidence allows NICE will provide guidance on how any treatments could be best targeted to those most likely to benefit. The intervention will be appraised according to its anticipated licence indication. The cost of strontium ranelate has yet to be determined. This appraisal covers the treatment of postmenopausal women with osteoporosis who have normal calcium levels and/or vitamin D levels.
Related NICE recommendations:	**In progress:** Technology Appraisal: The clinical effectiveness and cost effectiveness of technologies for the primary prevention of osteoporotic fragility fractures in postmenopausal women. Expected date of issue to be confirmed. Technology Appraisal: The clinical effectiveness and cost effectiveness of technologies for the secondary prevention of osteoporotic fractures in postmenopausal women. Expected date of issue October 2004. Technology Appraisal: Faller's clinics for the assessment and prevention of falls. Expected date of issue October 2005. Clinical guideline: Osteoporosis: assessment of fracture risk and the prevention of osteoporotic fractures in individuals at high risk. Expected date of issue February 2006. Clinical guideline: Falls: the assessment and prevention of falls in older people. Expected date of issue September 2004. **Completed:** None

[1] Remit from Department of Health: To appraise the clinical and cost effectiveness of strontium ranelate in its licensed indications for the prevention and treatment of osteoporosis.