NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Abaloparatide for preventing osteoporotic fractures in postmenopausal women

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of abaloparatide within its marketing authorisation for preventing osteoporotic fractures in postmenopausal women.

Background

Osteoporosis is a progressive skeletal disorder which is characterised by low bone mass and deterioration of the structure of bone tissue, leading to an increase in bone fragility and susceptibility to fracture.

Osteoporosis is diagnosed using scans that measure bone mineral density (BMD). The difference between the density of the person's bones and that of a healthy young adult is shown by the T-score. People are diagnosed with osteoporosis if their T-score is −2.5 standard deviations or below. More than 2 million people in England have osteoporosis[1]. Women are at a greater risk of developing osteoporosis than men because the decrease in oestrogen levels after menopause accelerates bone loss[2]. The prevalence of osteoporosis increases markedly with age, from 2% at 50 years to more than 25% at 80 years in women[3].

There may be no symptoms and osteoporosis often remains undiagnosed in people who have not had a fracture. Osteoporotic fragility fractures (fractures that occur from standing height or less) occur most commonly in the hip, vertebrae and wrist[4]. After a hip fracture, a high proportion of women are permanently unable to walk independently. Vertebral fractures are associated with curvature of the spine and height loss, which may result in pain, breathing difficulties and gastrointestinal problems. It is thought that the majority of vertebral fractures do not come to clinical attention[5, 6]. Both hip and vertebral fractures are also associated with increased mortality.

NICE Clinical Guideline 146, 'Osteoporosis: assessing the risk of fragility fracture' recommends that assessment of fracture risk should be considered:

- in all women aged 65 years and over
- in women aged under 65 years in the presence of risk factors.

Women who have not had a fracture may be offered treatment to prevent fractures (called primary prevention). NICE technology appraisal guidance

160 recommends alendronate as first-line treatment for the primary prevention of fragility fractures in postmenopausal women with osteoporosis who have an increased fracture risk defined by age, T-score, and number of independent clinical risk factors for fracture, or indicators of low BMD. For women who cannot take alendronate, NICE technology appraisal guidance 160 and 204 recommend risedronate, etidronate (discontinued in the UK), strontium ranelate or denosumab, at specified fracture risks, defined by age, T-score and number of independent clinical risk factors for fracture.

Women who have already had a fracture may be offered treatment to prevent further fractures (called secondary prevention). NICE technology appraisal guidance 161 recommends alendronate for secondary prevention of fragility fractures in post-menopausal women with confirmed osteoporosis. For women who cannot take alendronate, NICE technology appraisal guidance 161 recommends risedronate, etidronate (discontinued in the UK), raloxifene, strontium ranelate, and teriparatide at specified fracture risks, defined by age, T-score and number of independent clinical risk factors for fracture. NICE technology appraisal guidance 204 recommends denosumab as a treatment option for the secondary prevention of osteoporotic fragility fractures only in postmenopausal women at increased risk of fractures who are unable to comply with the special instructions for administering alendronate and either risedronate or etidronate, or have an intolerance of, or a contraindication to, those treatments.

After publication of NICE technology appraisal guidance 160 and 161, the marketing authorisation for strontium ranelate was changed to specify that it should be used only for postmenopausal women at high risk of fracture.

An ongoing NICE multiple technology appraisal is partially updating the recommendations in technology appraisals 160 and 161 and is also appraising ibandronate and zoledronate (ID782). Once this ongoing multiple technology appraisal is completed, NICE will conduct a further multiple technology appraisal of all non-bisphosphonates licensed for the prevention of osteoporotic fragility fractures.

The technology

Abaloparatide (brand name unknown, Radius Health) is a synthetic peptide analogue of human parathyroid hormone-related protein that stimulates new bone formation. Abaloparatide is administered subcutaneously.

Abaloparatide does not currently have a marketing authorisation in the UK for preventing osteoporotic fractures in postmenopausal women. It has been studied in a clinical trial compared with placebo for the prevention of fractures in postmenopausal women with severe osteoporosis. The clinical trial also included an active comparator (teriparatide).

Intervention(s)	Abaloparatide

Population(s)	Postmenopausal women at increased absolute risk of osteoporotic fracture
Comparators	For primary prevention: • bisphosphonates (such as alendronate, ibandronate, risedronate, zoledronate; subject to ongoing NICE technology appraisal [ID782]) • denosumab • strontium ranelate • best supportive care (for example, calcium and vitamin D supplements) For secondary prevention: • bisphosphonates (such as alendronate, ibandronate, risedronate, zoledronate; subject to ongoing NICE technology appraisal [ID782]) • denosumab • strontium ranelate • raloxifene • teriparatide • best supportive care (for example, calcium and vitamin D supplements)
Outcomes	The outcome measures to be considered include: • fractures • bone mineral density • mortality • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.

Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: 'Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women' (2008). NICE technology appraisal guidance 160. 'Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women' (2008). NICE technology appraisal guidance 161. 'Denosumab for the prevention of osteoporotic fractures in postmenopausal women' (2010). NICE technology appraisal guidance 204. Appraisals in development 'Bisphosphonates for preventing osteoporotic fragility fractures (including a partial update of NICE technology appraisal guidance 160 and 161)'. NICE technology appraisal guidance [ID782]. Publication to be confirmed. Related Guidelines: 'Osteoporosis: assessing the risk of fragility fracture' (2012). NICE Clinical Guideline 146. Related NICE Pathways: Osteoporosis (2012) NICE pathway, available at: http://pathways.nice.org.uk/pathways/osteoporosis
Related National Policy	Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014, domains 1–5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf

Questions for consultation

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process.

- An alternative option is to appraise abaloparatide within the proposed multiple technology appraisal of non-bisphosphonates for preventing osteoporotic fragility fractures. Which option would stakeholders prefer? The timing of the multiple technology appraisal has not been confirmed, but it is anticipated to begin in mid-2016.

- We welcome comments on the appropriateness of appraising this topic through the STA process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction)

What is the likely place of abaloparatide in the treatment pathway of osteoporosis in postmenopausal women?

Have all relevant comparators for abaloparatide been included in the scope? Which treatments are considered to be established clinical practice in the NHS for preventing osteoporotic fractures in postmenopausal women?

Are there any subgroups of people in whom abaloparatide is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider abaloparatide will fit into the existing NICE pathway, 'Osteoporosis'?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which abaloparatide will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider abaloparatide to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of abaloparatide can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

References

1 NICE technology appraisal guide 161 (2011). Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women (amended). Accessed July 2015.

2 NHS Choices (2014). Osteoporosis – Causes. Accessed July 2015.

3 NICE technology appraisal guide 160 (2011). Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women (amended). Accessed July 2015.

4 NHS Choices (2015). Osteoporosis – Introduction. Accessed July 2015.

5 Cooper C, Atkinson EJ, O'Fallon WM et al. (1992). Incidence of clinically diagnosed vertebral fractures: a population-based study in Rochester, Minnesota, 1985-1989. Journal of Bone and Mineral Research 7:221.

6 Meunier PJ, Delmas PD, Easstell R et al. (1999). Diagnosis and management osteoporosis in postmenopausal women: clinical guidelines. International Committee for Osteoporosis Clinical Guidelines. Clinical Therapeutics 21(6): 1025–1044.