NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Romosozumab for treating severe osteoporosis

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of romosozumab within its marketing authorisation for preventing osteoporotic fragility fractures in adults with severe osteoporosis at high risk of fracture.

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 risk of fracture.

Osteoporosis is asymptomatic and often remains undiagnosed in the absence of fracture. In the UK, it is estimated that around 3 million people have osteoporosis, which is defined as having a bone mineral density (BMD) that is 2.5 standard deviations or more below the average value for young healthy adults (usually referred to as a 'T-score' of -2.5 or lower). The prevalence of osteoporosis increases markedly with age. In women, decreased oestrogen levels after the menopause accelerate bone loss, increasing the risk of osteoporosis. Half of women and one-fifth of men over the age of 50 will break a bone, mostly as a result of low bone strength.[1] Osteoporosis can also be caused by the long-term systemic use of corticosteroids.

There are approximately 536,000 new fragility fractures in the UK per year.[2] Osteoporotic fragility fractures occur most commonly in the hip, vertebrae and wrist. After a hip fracture, a high proportion of people are permanently unable to walk independently or to perform other activities of daily living and, consequently, many are unable to live independently. Vertebral fractures can be associated with curvature of the spine and height loss, and can result in chronic pain, breathing difficulties, gastrointestinal problems and difficulties in performing activities of daily living. Both hip and vertebral fractures are associated with increased mortality.

Currently, related NICE guidance includes:

- NICE clinical guideline 146, 'Osteoporosis: assessing the risk of fragility fracture', which recommends:
    - considering the assessment of fracture risk in all women aged 65 years and over and all men aged 75 years and over
    - considering the assessment of fracture risk in women aged under 65 years and men aged under 75 years in the presence of risk factors
    - not routinely assessing fracture risk in people aged under 50 years unless they have major risk factors (for example, current or frequent recent use of systemic corticosteroids, untreated premature menopause or previous fragility fracture)

  - estimating absolute fracture risk when assessing risk of fracture (for example, the predicted risk of major osteoporotic or hip fracture over 10 years, expressed as a percentage) using either FRAX or QFracture.[3,4]

- NICE technology appraisal 464, which recommends oral bisphosphonates (alendronic acid, ibandronic acid and risedronate sodium) and intravenous bisphosphonates (ibandronic acid and zoledronic acid) as options for treating osteoporosis in people who are eligible for risk assessment as defined in NICE clinical guideline 146 on osteoporosis, depending on the person's risk of fragility fracture. However, the risk level at which oral bisphosphonates are cost effective is not a clinical intervention threshold. This technology appraisal guidance should be applied clinically in conjunction with the NICE quality standard 149 on osteoporosis that defines the clinical intervention thresholds. These thresholds are based on the NICE-accredited National Osteoporosis Guideline Group guideline.

- NICE technology appraisal 204, which recommends denosumab:

  - for the primary prevention of fragility fractures in postmenopausal women at specified fracture risks, defined by age, T-score and number of independent clinical risk factors for fracture, who have osteoporosis and who cannot take alendronate and either risedronate or etidronate

  - for the secondary prevention of osteoporotic fragility fractures in postmenopausal women at increased risk of fractures who cannot take alendronate and either risedronate or etidronate.

- NICE technology appraisal 161, which recommends raloxifene, strontium ranelate (currently discontinued) and teriparatide at specified fracture risks defined by age, T-score and either number of independent clinical risk factors for fracture (raloxifene), or number of fractures (teriparatide). These recommendations are for women who have already sustained a fracture and who cannot take alendronate or risedronate.

The technology

Romosozumab (Evenity, UCB) is a monoclonal antibody that inhibits the protein sclerostin, increasing bone formation and decreasing bone breakdown. It is administered as a subcutaneous injection. It has a marketing authorisation in the UK for treating severe osteoporosis in postmenopausal women at high risk of fracture. It has been studied in clinical trials in postmenopausal women and men with osteoporosis.

Intervention(s)	Romosozumab
Population(s)	Adults with severe osteoporosis at high risk of fracture
Comparators	• Bisphosphonates (alendronic acid, risedronate sodium, ibandronic acid and zoledronic acid) • Non-bisphosphonates (denosumab, raloxifene and

	teriparatide) • No active treatment
Outcomes	The outcome measures to be considered include: • osteoporotic fragility fracture • 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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.
Other considerations	If evidence allows, subgroups based on patient characteristics that increase the risk of fracture (that is, those specified in NICE clinical guideline 146) or that affect the impact of fracture on lifetime costs and outcomes should be considered. The availability and cost of biosimilar and generic products should be taken into account. 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:** 'Bisphosphonates for treating osteoporosis' (2017). NICE Technology Appraisal 464. Review date 2022. 'Denosumab for the prevention of osteoporotic fractures in postmenopausal women' (2010). NICE Technology Appraisal 204. Reviewed 2014 'Raloxifene and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women'

	(2008, updated 2018). NICE Technology Appraisal 161 'Raloxifene for the primary prevention of osteoporotic fragility fractures in postmenopausal women' (2008, updated 2018). NICE Technology Appraisal 160 **Related Guidelines:** Osteoporosis: assessing the risk of fragility fracture (2012, updated 2017) NICE guideline CG146. Reviewed 2019 **Related Quality Standards:** Osteoporosis (2017) NICE quality standard 149 **Related NICE Pathways:** Osteoporosis (2021) NICE pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 2 and 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for romosozumab been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for severe osteoporosis?

Are the outcomes listed appropriate?

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

Where do you consider romosozumab 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 romosozumab is 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 romosozumab 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 romosozumab 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

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

References

1. Age UK (2020) Osteoporosis. Accessed February 2021

2. Compston J et al. (2017) UK clinical guideline for the prevention and treatment of osteoporosis. Archives of Osteoporosis 12(1): 43

3. FRAX, the World Health Organisation (WHO) fracture assessment tool, is available from https://www.sheffield.ac.uk/FRAX/. It can be used for people aged between 40 and 90 years, either with or without BMD values, as specified.

4. QFracture is available from https://qfracture.org/. It can be used for people aged between 30 and 84 years. BMD values cannot be incorporated into the risk algorithm.