Health Technology Briefing
October 2022

Denosumab biosimilar for treating postmenopausal osteoporosis

Company/Developer	Teva Pharmaceuticals Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 31131	NICE ID: 11807	UKPS ID: Not Available

Licensing and Market Availability Plans

Currently in phase III clinical trials

Summary

Denosumab biosimilar is in clinical development for the treatment of postmenopausal women with osteoporosis. Osteoporosis is a condition that causes weakening of the bones, which can result in increased risk of fractures or breaks. Women are at increased risk of osteoporosis because the female hormone, oestrogen, drops significantly after menopause, resulting in a rapid decrease of bone density. The patients affected by osteoporosis perceive it as a disease affecting their personal life with undesirable consequences such as chronic pain, impaired physical ability, reduced social activity, poor well-being, and depressed mood. The treatment of osteoporosis and prevention of fractures are vital for improving patients' health and reducing hospital burden.

Denosumab biosimilar has a similar form and function to denosumab, which is licensed for the treatment of osteoporosis in postmenopausal women. Denosumab is a monoclonal antibody (a type of protein) designed to recognise and attach to a specific protein (antigen) called RANKL. By attaching to and blocking RANKL, denosumab reduces the formation and activity of cells in the body that are involved in breaking down bone tissue, thereby reducing the loss of bone and maintaining bone strength, making fractures less likely to happen. Denosumab biosimilar is administered subcutaneously. If licenced, denosumab biosimilar would offer an additional treatment option for women with postmenopausal osteoporosis.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.
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Proposed Indication

Women, aged 60 to 90 years old, with postmenopausal osteoporosis.[1]

Technology

Description

Denosumab biosimilar (TVB-009; TVB-009P) contains the active ingredient denosumab, which is a human IgG2 monoclonal antibody that binds with high affinity to human receptor activator of nuclear factor-κB ligand (RANKL) and blocks binding of RANKL to RANK. The interaction of RANK with its ligand (RANKL) has been identified as the final common pathway through which bone resorption is regulated.[1-3] By binding to its receptor RANK on osteoclastic precursors, RANKL controls the differentiation, proliferation, and survival of osteoclasts.[3] Denosumab effectively blocks the interaction between RANKL and RANK, thereby inhibiting the formation of osteoclasts and enhancing bone strength. Bone loss is prevented through the inhibition of osteoclasts.[4]

Denosumab biosimilar is in clinical development for treating postmenopausal women with osteoporosis. In the phase III clinical trial (NCT04729621), denosumab biosimilar is administered subcutaneously as a 60mg/ml (1ml) solution for injection prefilled syringe (PFS) at weeks 1 and 26, and at week 52 in patients that were randomised to denosumab biosimilar in the main treatment period.[1]

Key Innovation

Denosumab is indicated for the treatment of osteoporosis in postmenopausal women by significantly reducing the risk of vertebral, non-vertebral and hip fractures.[5]

If licensed, denosumab biosimilar would offer an additional treatment option for postmenopausal women, through a similar form and function as denosumab.

Regulatory & Development Status

Denosumab biosimilar does not currently have Marketing Authorisation in the EU/UK for any indication.

Patient Group

Disease Area and Clinical Need

Osteoporosis is a condition that weakens bones, making them more fragile and likely to fracture and/or break. This results in common injuries, such as a fractured or broken wrist, hip, or vertebrate. Osteoporosis is not usually painful until a bone is broken, which is often the first sign. Some older people may develop the characteristic stooped (bent forward) posture, which happens when the bones in the spine have broken, making it difficult to support the weight of the body.[6] Risk factors for developing osteoporosis include hormone disorders; a family history of osteoporosis; a body mass index (BMI) of ≤19; long-term use of high-dose steroid tablets; eating disorders; heavy drinking and smoking; rheumatoid arthritis; malabsorption issues; long periods of inactivity; and taking some medicines used to treat breast and prostate cancers that can affect hormone levels. Women are more at risk of developing osteoporosis than men because oestrogen levels fall after menopause, leading to a rapid decrease in bone density.[7] The prevalence of osteoporosis in women increases significantly, from approximately 2% at 50 years of age to almost 50% at 80 years of age.[8] Postmenopausal osteoporosis can affect quality of life resulting in chronic pain, impaired physical ability, reduced social activity, poor wellbeing, and depressed mood.[9]

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In England and Wales, more than 2 million women have osteoporosis (2021).[8] In England, in 2021-22, there were 1,264 finished consultant episodes (FCE) for postmenopausal osteoporosis with pathological fracture, and postmenopausal osteoporosis (ICD-10 codes M80.0 and M81.0), resulting in 160 FCE bed days and 1,215 day cases.[10]

Recommended Treatment Options

NICE recommends the following treatment options:[11-15]

- Romosozumab for severe osteoporosis in people after menopause who are at high risk of fracture
- Bisphosphonates such as alendronic acid, ibandronic acid, risedronate sodium and zoledronic acid for treating osteoporosis
- Raloxifene and teriparatide for preventing osteoporotic fragility fractures in postmenopausal women who have osteoporosis
- Raloxifene for the primary prevention of osteoporotic fragility fractures in postmenopausal women
- Denosumab for preventing osteoporotic fragility fractures in postmenopausal women

Clinical Trial Information

Trial	NCT04729621; A Randomised, Double-Blind, Multinational, Multicentre Study to Compare Efficacy, Safety, and Immunogenicity of TVB-009P and Denosumab (Prolia®) in Patients With Postmenopausal Osteoporosis **Phase III** – Active, not recruiting **Location(s):** USA **Primary completion date:** June 2023
Trial Design	Randomised, quadruple-masked, parallel assignment
Population	N=326 (estimated); postmenopausal women aged ≥60 years to ≤90 years old.
Intervention(s)	• Main treatment period: Denosumab biosimilar (SC) 60mg/ml (1ml) prefilled syringe (PFS) administered at weeks 1 and 26. • Transition period: Denosumab biosimilar (SC) 60mg/ml (1ml) PFS administered at week 52 in patients that were randomised to denosumab biosimilar in the main treatment period.
Comparator(s)	Denosumab (Prolia®) (SC) 60mg/ml (1ml) prefilled syringe (PFS)
Outcome(s)	Primary outcome measure: Percent change from baseline in lumbar spine bone mineral density (LS-BMD) at week 52 [Time Frame: Baseline and week 52] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

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Estimated Cost

The cost of denosumab biosimilar is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance. Romosozumab for treating severe osteoporosis (TA791). May 2022.
- NICE technology appraisal guidance. Bisphosphonates for treating osteoporosis (TA464). August 2017.
- NICE technology appraisal guidance. Denosumab for the prevention of osteoporotic fractures in postmenopausal women (TA204). October 2010.
- NICE technology appraisal guidance. Raloxifene and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women (TA161). October 2008.
- NICE technology appraisal guidance. Raloxifene for the primary prevention of osteoporotic fragility fractures in postmenopausal women (TA160). October 2008.
- NICE clinical guideline in development. Osteoporosis: assessing the risk of fragility fracture (GID-NG10216). Expected publication date: February 2024.
- NICE clinical guideline. Osteoporosis: assessing the risk of fragility fracture (CG146). August 2012.
- NICE quality standard. Osteoporosis (QS149). April 2017.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/2014. NHS Standard Contract for Specialised Rheumatology Services (Adult). A13/S/a.

Other Guidance

- National Osteoporosis Guideline Group (NOGG) UK. Clinical guideline for the prevention and treatment of osteoporosis (NOGG 2021). September 2021.[16]
- International Osteoporosis Foundation (IOF), and the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO). European guidance for the diagnosis and management of osteoporosis in postmenopausal women. October 2018.[17]

Additional Information

Teva Pharmaceuticals Ltd did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

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