Medicines & Healthcare products
Regulatory Agency

Public Assessment Report

National Procedure

Conexxence 60 mg solution for injection in pre-filled syringe

denosumab

PL 08828/0381

Fresenius Kabi Limited

LAY SUMMARY

Conexxence 60 mg solution for injection in pre-filled syringe
denosumab

This is a summary of the Public Assessment Report (PAR) for Conexxence 60 mg solution for injection in pre-filled syringe. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

This product will be referred to as Conexxence in this lay summary for ease of reading.

This application was approved under International Recognition procedure (IRP). The Reference Regulator (RR) was the European Medicines Agency (EMA), with the procedure number (EMEA/H/C/006268/0000). The procedure followed route A.

This application was approved under Regulation 53B of the Human Medicines Regulation 2012, as amended (previously Article 10.4 of Directive 2001/83/EC, as amended).

For practical information about using Conexxence, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Conexxence and what is it used for?
This product is a biosimilar medicine, this is biological medicine which is similar to and considered interchangeable with a reference medicine already authorised, called Prolia 60 mg solution for injection in pre-filled syringe.

Conexxence is used to treat:

- osteoporosis in women after the menopause (postmenopausal) and men who have an increased risk of fracture (broken bones), reducing the risk of spinal, non-spinal and hip fractures.
- bone loss that results from a reduction in hormone (testosterone) level caused by surgery or treatment with medicines in patients with prostate cancer.
- bone loss that results from long-term treatment with glucocorticoids in patients who have an increased risk of fracture.

How does Conexxence work?
Conexxence contains denosumab, a protein (monoclonal antibody) that interferes with the action of another protein, in order to treat bone loss and osteoporosis. Treatment with Conexxence makes bone stronger and less likely to break.

Bone is a living tissue and is renewed all the time. Oestrogen helps keep bones healthy. After the menopause, oestrogen level drops which may cause bones to become thin and fragile. This can eventually lead to a condition called osteoporosis. Osteoporosis can also occur in men due to a number of causes including ageing and/or a low level of the male hormone, testosterone. It can also occur in patients receiving glucocorticoids. Many patients with osteoporosis have no symptoms, but they are still at risk of breaking bones, especially in the spine, hips and wrists.

Surgery or medicines that stop the production of oestrogen or testosterone used to treat patients with breast or prostate cancer can also lead to bone loss. The bones become weaker and break more easily.

How is Conexxence used?
The pharmaceutical form of this medicine is a solution for injection and the route of administration is subcutaneous (under the skin) use.

The recommended dose is one pre-filled syringe of 60 mg administered once every 6 months, as a single injection under the skin (subcutaneous). The best places to inject are the top of your thighs and the abdomen. The patient's carer can also use the outer area of their upper arm. The patient should consult their doctor on the date for a potential next injection.

The patient should also take calcium and vitamin D supplements while being on treatment with Conexxence. Their doctor will discuss this with them.

The patient's doctor may decide that it is best for them or a carer to inject Conexxence. Their doctor or healthcare provider will show the patient or their carer how to use Conexxence. For instructions on how to inject Conexxence, refer the section at the end of the PIL.

For further information on how Conexxence is used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should ask the administering healthcare practitioner if they have any questions concerning their medicine.

What benefits of Conexxence have been shown in studies?
Laboratory studies comparing Conexxence with Prolia have shown that the active substance in Conexxence is highly similar to that in Prolia in terms of structure, purity and biological activity. Studies have also shown that giving Conexxence produces similar levels of the active substance in the body to those seen with Prolia.

In addition, a study involving 553 women with osteoporosis who have been through the menopause compared the effectiveness of Conexxence with that of Prolia. After a year of treatment, bone mineral density in the spine (a measure of how strong the bones are) increased by around 5.7% in women who received Conexxence and 5.1% in those who received Prolia.

Because Conexxence is a biosimilar medicine, the studies on the effectiveness carried out with Prolia do not all need to be repeated for Conexxence.

What are the possible side effects of Conexxence?
For the full list of all side effects reported with this medicine, see Section 4 of the PIL or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card

scheme at https://yellowcard.mhra.gov.uk or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

The most common side effects with Conexxence (which may affect more than 1 in 10 people) are bone, joint, and/or muscle pain which is sometimes severe, and arm or leg pain (pain in extremity).

Why was Conexxence approved?
It was concluded that, Conexxence has been shown to be similar to the reference medicine. Therefore, the MHRA decided that, as for the reference medicine, the benefits are greater than the risks and recommended that it can be approved for use.

Conexxence has been authorised with the condition to perform further studies and/or to provide additional measures to minimise the risk. See section below "What measures are being taken to ensure the safe and effective use of Conexxence?"

What measures are being taken to ensure the safe and effective use of Conexxence?
As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Conexxence. The RMP details the important risks of Conexxence, how these risks can be minimised, any uncertainties about Conexxence (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Conexxence:

Safety Concerns	
Important identified risks	• Hypocalcaemia • Skin infection leading to hospitalization • Osteonecrosis of the jaw • Hypersensitivity reactions • Atypical femoral fracture • Hypercalcemia in paediatric patients receiving denosumab and after treatment discontinuation
Important potential risks	• Fracture healing complications • Infection • Cardiovascular events • Malignancy
Missing information	• None

The Marketing Authorisation Holder has committed to additional risk minimisation measures which include provision of educational materials, such as Patient Reminder Card.

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Conexxence are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

Other information about Conexxence

A marketing authorisation for Conexxence was granted in the United Kingdom on 12 August 2025.

The full PAR for Conexxence follows this summary.

This summary was last updated in October 2025.

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I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Conexxence 60 mg solution for injection in pre-filled syringe (PL 08828/0381) could be approved.

The product is approved for the following indications:
Treatment of osteoporosis in postmenopausal women and in men at increased risk of fractures. In postmenopausal women denosumab significantly reduces the risk of vertebral, non-vertebral and hip fractures.

Treatment of bone loss associated with hormone ablation in men with prostate cancer at increased risk of fractures. In men with prostate cancer receiving hormone ablation, denosumab significantly reduces the risk of vertebral fractures.

Treatment of bone loss associated with long-term systemic glucocorticoid therapy in adult patients at increased risk of fracture.

Mechanism of action
Denosumab is a human monoclonal antibody (IgG2) that targets and binds with high affinity and specificity to RANKL, preventing activation of its receptor, RANK, on the surface of osteoclast precursors and osteoclasts. Prevention of the RANKL/RANK interaction inhibits osteoclast formation, function and survival, thereby decreasing bone resorption in cortical and trabecular bone.

This application was approved under International Recognition procedure (IRP). The Reference Regulator (RR) was the European Medicines Agency (EMA), with the procedure number (EMEA/H/C/006268/0000). For the scientific discussion of the quality, non-clinical and clinical assessment conducted by the reference regulator, please refer to the public assessment report on the relevant competent authority's website.

This application was approved under Regulation 53B of the Human Medicines Regulation 2012, as amended (previously Article 10.4 of Directive 2001/83/EC, as amended).

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

A marketing authorisation for Conexxence 60 mg solution for injection in pre-filled syringe was granted on 12 August 2025.

II. PRODUCT INFORMATION

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

The SmPC is in line with current guidelines and is satisfactory.

PATIENT INFORMATION LEAFLET (PIL)

The PIL is in line with current guidelines and is satisfactory.

LABEL

The labelling is in line with current guidelines and is satisfactory.

III. QUALITY ASPECTS

MHRA considered that the quality data submitted for this application is satisfactory.

The grant of a marketing authorisation was recommended.

IV. NON-CLINICAL ASPECTS

MHRA considered that the non-clinical data submitted for this application is satisfactory.

The grant of a marketing authorisation was recommended.

V. CLINICAL ASPECTS

MHRA considered that the clinical data submitted for this application is satisfactory.

The grant of a marketing authorisation was recommended.

VI. RISK MANAGEMENT PLAN (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. In addition to routine pharmacovigilance and risk minimisation measures, additional risk minimisation measures have been proposed (see table below for the risk minimisation measures and pharmacovigilance activities for all safety concerns):

Important identified risk: Hypocalcaemia	
Evidence for linking the risk to the medicine	The source of information is clinical/safety and postmarketing data of the reference product Amgen Prolia (EU-RMP v31.0, 2023) and medical literature.
Risk factors and risk groups	Risk factors include severe renal impairment and hyperphosphatemia. Other risks factors may include a history of hypoparathyroidism, parathyroid hormone resistance, vitamin D deficiency or resistance, thyroid surgery, parathyroid surgery, malabsorption syndromes, excision of small intestine, severe renal impairment (creatinine clearance <30 mL/min), dialysis, and some medications (Finkelstein 2001).
Risk minimization measures	**Routine risk communication:** SmPC: Section 4.2, Section 4.3, Section 4.4, Section 4.8 PIL: Section 2, Section 4 **Routine risk minimization activities recommending specific clinical measures to address the risk:**

	Recommendation for correction of hypocalcaemia prior to initiating treatment with Conexxence and clinical monitoring of calcium levels during treatment with Conexxence is included in SmPC Section 4.4. **Other risk minimization measures beyond the Product Information:** Medicine's legal status: prescription only medicine. **Additional risk minimization measures:** None
Additional pharmacovigilance activities	None
Important identified risk: Skin infection leading to hospitalization	
Evidence for linking the risk to the medicine	The source of information is clinical/safety data of the reference product Amgen Prolia (EU-RMP v31.0, 2023) and medical literature.
Risk factors and risk groups	Risk factors for infection in general include increasing age, immunosuppression associated with cancer, diabetes, HIV/ AIDS, immunosuppressant drugs (e.g., corticosteroids, arthritis medications, and chemotherapy drugs), substance abuse, and malnutrition. Risk factors for skin infection in older patients include skin wounds, peripheral vascular disease, eczema/dermatitis, and venous stasis disorders.
Risk minimization measures	**Routine risk communication:** SmPC: Section 4.4, Section 4.8. PIL: Section 2, Section 4. **Routine risk minimization activities recommending specific clinical measures to address the risk:** None **Other risk minimization measures beyond the Product Information:** Medicine's legal status: prescription only medicine. **Additional risk minimization measures:** None
Additional pharmacovigilance activities	None
Important identified risk: Osteonecrosis of the jaw	
Evidence for linking the risk to the medicine	The source of information is clinical/safety data of the reference product Amgen Prolia (EU-RMP v31.0, 2023) and medical literature.
Risk factors and risk groups	Risk factors include duration of exposure to denosumab, prior bisphosphonate use (particularly for extended periods of time), older age, periodontal disease, dentoalveolar surgery, trauma from poorly fitting dentures, malignancy, chemotherapy, corticosteroids, smoking, systemic or regional infection, immune-compromised state predisposing to increased risk of infection, hypercoagulable state secondary to underlying malignancy, and vascular insufficiency due to thrombosis (Mehrotra and Ruggiero 2006, Ruggiero et al. 2006).
Risk minimization measures	**Routine risk communication:** SmPC: Section 4.4, Section 4.8 PIL: Section 2, Section 4

	Routine risk minimization activities recommending specific clinical measures to address the risk: Recommendations for oral examination, maintenance of good oral hygiene during treatment, management of patients with unavoidable invasive dental procedure, and temporary interruption of treatment if ONJ occurs are included in Section 4.4 of SmPC. **Other risk minimization measures beyond the Product Information:** Medicine's legal status: prescription only medicine. **Additional risk minimization measures:** Patient Reminder Card
Additional pharmacovigilance activities	None
Important identified risk: Hypersensitivity reactions	
Evidence for linking the risk to the medicine	The source of information is postmarketing data of the reference product Amgen Prolia (EU-RMP v31.0, 2023).
Risk factors and risk groups	Known hypersensitivity to denosumab and any of its excipients.
Risk minimization measures	**Routine risk communication:** SmPC: Section 4.3, Section 4.8. PIL: Section 2, Section 4. **Routine risk minimization activities recommending specific clinical measures to address the risk:** None. **Other risk minimization measures beyond the Product Information:** Medicine's legal status: prescription only medicine. **Additional risk minimization measures:** None
Additional pharmacovigilance activities	None
Important identified risk: Atypical femoral fracture	
Evidence for linking the risk to the medicine	The source of information is clinical/safety data of the reference product Amgen Prolia (EU-RMP v31.0, 2023) and medical literature.
Risk factors and risk groups	Long-term antiresorptive treatment has been associated with AFF. Corticosteroids have also been reported in the literature to potentially be associated with AFF (Giusti et al. 2011, Meier et al. 2012). Atypical femoral fractures have also been reported in patients with certain comorbid conditions (e.g., vitamin D deficiency, RA, hypophosphatasia) and with use of bisphosphonates, glucocorticoids, and proton pump inhibitors (Shane et al. 2010).
Risk minimization measures	**Routine risk communication**: SmPC: Section 4.4, Section 4.8. PIL: Section 2, Section 4. **Routine risk minimization activities recommending specific clinical measures to address the risk**:

	Recommendation for reporting new or unusual thigh, hip, or groin pain is included Section 4.4 of SmPC. **Other risk minimization measures beyond the Product Information**: Medicine's legal status: prescription only medicine. **Additional risk minimization measures:** None
Additional pharmacovigilance activities	None
Important identified risk: Hypercalcemia in paediatric patients receiving denosumab and after treatment discontinuation	
Evidence for linking the risk to the medicine	The source of information is clinical/safety and postmarketing data of the reference product Amgen Prolia (EU-RMP v31.0, 2023).
Risk factors and risk groups	Paediatric patients with growing skeletons and high bone turnover disease states (such as OI).
Risk minimization measures	**Routine risk communication:** SmPC: Section 4.2, Section 4.4, Section 4.8. PIL: Section 2. **Routine risk minimization activities recommending specific clinical measures to address the risk:** None. **Other risk minimization measures beyond the Product Information:** Medicine's legal status: prescription only medicine. **Additional risk minimization measures:** None
Additional pharmacovigilance activities	None
Important potential risk: Fracture healing complications	
Evidence for linking the risk to the medicine	This is a theoretical risk based on the mechanism of action (Amgen Prolia EU-RMP v31.0, 2023).
Risk factors and risk groups	General risk factors for fracture healing complications are thought to include older age, diabetes, use of medications such as non-steroidal anti-inflammatory drugs and corticosteroids, smoking, excessive alcohol use, and poor nutrition (Gaston and Simpson 2007, Hernandez et al. 2012).
Risk minimization measures	**Routine risk communication:** SmPC: Section 5.3. **Routine risk minimization activities recommending specific clinical measures to address the risk:** None. **Other risk minimization measures beyond the Product Information:** Medicine's legal status: prescription only medicine. **Additional risk minimization measures:** None

Additional pharmacovigilance activities	None
Important potential risk: Infection	
Evidence for linking the risk to the medicine	This is considered a potential risk based on theoretical concerns which has not been substantiated in the Amgen's extensive clinical study program or in the postmarketing experience (Amgen Prolia EU-RMP v31.0, 2023).
Risk factors and risk groups	Risk factors for infection in general include increasing age, immunosuppression associated with cancer, diabetes, HIV/AIDS, immunosuppressant drugs (e.g., corticosteroids, arthritis medications, and chemotherapy drugs), substance abuse, and malnutrition.
Risk minimization measures	**Routine risk communication:** SmPC: Section 4.8. PIL: Section 4. **Routine risk minimization activities recommending specific clinical measures to address the risk:** None. **Other risk minimization measures beyond the Product Information:** Medicine's legal status: prescription only medicine. **Additional risk minimization measures:** None
Additional pharmacovigilance activities	None
Important potential risk: Cardiovascular events	
Evidence for linking the risk to the medicine	This is a theoretical risk based on epidemiological data demonstrating elevated OPG in patients with cardiovascular disease (Amgen Prolia EU-RMP v31.0, 2023).
Risk factors and risk groups	The denosumab development program comprises studies of older subject populations (e.g., osteoporosis, cancer) that are likely to have a higher incidence of pre-existing cardiovascular conditions and, thus, a higher incidence of cardiovascular toxicities than that of the general population (Hak et al. 2000, Schulz et al. 2004)
Risk minimization measures	**Routine risk communication:** None **Routine risk minimization activities recommending specific clinical measures to address the risk:** None **Other risk minimization measures beyond the Product Information:** Medicine's legal status: prescription only medicine. **Additional risk minimization measures:** None
Additional pharmacovigilance activities	None
Important potential risk: Malignancy	

Evidence for linking the risk to the medicine	This is considered a potential risk based on theoretical concerns and has not been substantiated in the extensive Amgen's clinical study program or in the postmarketing experience (Amgen Prolia EU-RMP v31.0, 2023).
Risk factors and risk groups	General factors for risk of malignancy include advancing age, diet, cigarette smoking, excessive ethanol consumption, and numerous environmental toxins. In addition, cancer populations are at increased risk for a second primary malignancy because of their existing malignancy, possible genetic predisposition, and exposure to chemotherapy and radiation treatment (Anand et al. 2008, WHO 2011).
Risk minimization measures	**Routine risk communication:** None **Routine risk minimization activities recommending specific clinical measures to address the risk:** None **Other risk minimization measures beyond the Product Information:** Medicine's legal status: prescription only medicine. **Additional risk minimization measures:** None
Additional pharmacovigilance activities	None
Missing information: None	

This is acceptable.

VII. USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) was provided with the application in accordance with legal requirements, including user consultation.

VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The benefit/risk balance is, therefore, considered to be positive.

Conexxence has been authorised with the condition to perform further studies and/or to provide additional measures to minimise the risk. The Marketing Authorisation Holder shall complete, within the stated timeframe, the following measures:

Description	Due date
Additional Risk Minimisation Measure The MAH shall ensure that the following educational material regarding osteonecrosis of the jaw is implemented: – Patient Reminder Card (PRC) on the risk of osteonecrosis of the jaw The PRC is aimed at ensuring user awareness of the risk of developing osteonecrosis of the jaw and the necessary precautions required to help manage this risk. The key elements included within the materials are detailed in the RMP (Annex 6).	Must be implemented prior to launch

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory.

In accordance with legal requirements, the current approved UK version of the SmPC and PIL for this product are available on the MHRA website.

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Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations, where significant changes are made, are recorded on the MHRA website or Reference Regulator (RR) website. Minor changes to the marketing authorisation are recorded in the current SmPCs and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**