Medicines & Healthcare products
Regulatory Agency

Public Assessment Report

National Procedure

Jubbonti 60 mg solution for injection in pre-filled syringe

denosumab

PLGB 04416/1709

Sandoz Limited

LAY SUMMARY

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

This is a summary of the Public Assessment Report (PAR) for Jubbonti 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 Jubbonti 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/005964/0000). The procedure followed route A.

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

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

What is Jubbonti and what is it used for?
This product is a biosimilar (similar biological) medicine. This means that this medicine is similar to 'biological' reference medicine already authorised in the European Union (EU), called Prolia 60 mg/ml solution for injection.

Jubbonti 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 Jubbonti work?
Jubbonti contains denosumab, a protein (monoclonal antibody) that interferes with the action of another protein, in order to treat bone loss and osteoporosis. Treatment with Jubbonti 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 Jubbonti used?
The pharmaceutical form of this medicine is a solution for injection, and the route of administration is for 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 thighs and the abdomen. The patient's caregiver can also use the outer area of their upper arm. The patient or caregiver should consult their doctor on the date for a potential next injection. Each pack of Jubbonti contains a calendar card with a sticker that can be used to keep a record of the next injection date.

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

A doctor may decide that it is best for the patient or a caregiver to inject Jubbonti. The patient's doctor or healthcare provider will show them or their caregiver how to use Jubbonti.

Due to the high-level of detail in the usage instructions it is best to refer directly to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website, for information on how Jubbonti is used.

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 Jubbonti have been shown in studies?
Laboratory studies comparing Jubbonti with the reference medicines, Prolia, have shown that the active substance in Jubbonti is highly similar to that in Prolia in terms of structure, purity and biological activity. A study has also shown that giving Jubbonti produces similar levels of the active substance in the body to giving Prolia.

In addition, a study involving 463 women with osterporosis who have been through the menopause showed that Jubbonti is as effective as Prolia at increasing bone mineral density (a measure of how strong the bones are) in the spine. After a year of treatment, bone mineral density increased by around 5% in both women who received Jubbonti and those who received Prolia.

Because Jubbonti is a biosimilar medicine, the studies on the effectiveness and safety of denosumab carried out with Prolia do not all need to be repeated for Jubbonti.

What are the possible side effects of Jubbonti?
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.

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

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

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

The following safety concerns have been recognised for Jubbonti:

Important identified risks	Hypocalcemia Skin infection leading to hospitalization Osteonecrosis of the jaw Hypersensitivity reactions Atypical femoral fracture Hypercalcemia in pediatric 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 patient reminder card (PRC) on the risk of osteonecrosis of the jaw.

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 Jubbonti 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 Jubbonti

A marketing authorisation was granted in the United Kingdom on 07 November 2024.

The full PAR for Jubbonti follows this summary.

This summary was last updated in December 2024.

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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 Jubbonti 60 mg solution for injection in pre-filled syringe (PLGB 04416/1709) 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.

Jubbonti 60 mg solution for injection in pre-filled syringe contains the active substance, denosumab which 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/005964/0000). 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 EMA website.

This application was approved under Regulation 53 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 was granted on 07 November 2024.

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: Hypocalcemia

Evidence for linking the risk to the medicine	This risk was identified in the phase 3, randomized, double-blind, placebo- or active-controlled studies with originator drug (Prolia).
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.
Risk minimization measures	Routine risk minimization measures: • SmPC Section 4.4, where recommendation regarding correction and monitoring of calcium levels is provided • SmPC Sections 4.2, 4.3, 4.4 and 4.8 • PL Sections 2, 3 and 4 Additional risk minimization measures: • None

Important identified risk: Skin infection leading to hospitalization

Evidence for linking the risk to the medicine	This risk was identified in the phase 3, randomized, double-blind, placebo- or active-controlled studies with originator drug (Prolia).
Risk factors and risk groups	Risk factors for infection in general include increasing age, immunosuppression associated with cancer, diabetes, human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (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 minimization measures: • SmPC Sections 4.4, and 4.8 • PL Sections 2 and 4 Additional risk minimization measures: • None

Important identified risk: Osteonecrosis of the jaw

Evidence for linking the risk to the medicine	This risk was identified in open-label long-term extensions to phase 3, randomized, double-blind, placebo-controlled studies with originator drug (Prolia).
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.
Risk minimization measures	Routine risk minimization measures: • SmPC Section 4.4, where oral hygiene and dental management guidance is provided • SmPC Sections 4.4, 4.8 and 5.1 • PL Sections 2 and 4 Additional risk minimization measures: • Patient reminder card

Important identified risk: Hypersensitivity reactions

Evidence for linking the risk to the medicine	This risk was identified in the postmarketing setting based on a clinically plausible association between administration of denosumab and hypersensitivity reactions with originator drug (Prolia).
Risk factors and risk groups	Known hypersensitivity to denosumab and any of its excipients.
Risk minimization measures	Routine risk minimization measures: • SmPC Sections 4.3 and 4.8 • PL Sections 2 and 4 Additional risk minimization measures: • None

Important identified risk: Atypical femoral fracture

Evidence for linking the risk to the medicine	This risk was identified in open-label long-term extensions to phase 3, randomized, double-blind, active-controlled study with originator drug (Prolia).
Risk factors and risk groups	Long-term antiresorptive treatment has been associated with atypical femoral fracture. Corticosteroids have also been reported in the literature to potentially be associated with atypical femoral fracture. Atypical femoral fractures have also been reported in patients with certain comorbid conditions (e.g., vitamin D deficiency, rheumatoid arthritis, hypophosphatasia) and with use of bisphosphonates, glucocorticoids, and proton pump inhibitors.
Risk minimization measures	Routine risk minimization measures: SmPC Section 4.4, where recommendation for reporting potential symptoms is provided • SmPC Sections 4.4, 4.8 and 5.1 • PL Sections 2 and 4 Additional risk minimization measures: • None

Important identified risk: Hypercalcemia in pediatric patients receiving denosumab and after treatment discontinuation

Evidence for linking the risk to the medicine	Data to evaluate safety concerns were derived from Prolia clinical studies in pediatric subjects with osteogenesis imperfecta, XGEVA clinical studies and postmarketing adverse event reporting involving pediatric patients receiving denosumab at unapproved doses and/or unapproved indications for use.
Risk factors and risk groups	Pediatric patients with growing skeletons and high bone turnover disease states (such as osteogenesis Imperfecta).
Risk minimization measures	Routine risk minimization measures: • SmPC Sections 4.2, 4.4, 4.8 and 5.1 Additional risk minimization measures: • None

Important identified risk: Fracture healing complications

Evidence for linking the risk to the medicine	This is a theoretical risk based on the potential mechanism of action with denosumab.
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.
Risk minimization measures	Routine risk minimization measures: • None

	Additional risk minimization measures: • None

Important identified 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 extensive clinical study program or in the postmarketing experience of Prolia.
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 minimization measures: • SmPC Section 4.8 • PL Section 4 Additional risk minimization measures: • 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 osteoprotegerin in patients with cardiovascular disease of Prolia.
Risk factors and risk groups	The denosumab development program comprised 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. Risk factors for atherosclerosis include age, sex, ethnicity, family history, elevated lipid levels, cigarette smoking, hypertension, diabetes, and concomitant medications, including antipsychotic agents and COX-2 inhibitors.
Risk minimization measures	Routine risk minimization measures: • None Additional risk minimization measures: • 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 clinical study program or in the postmarketing experience with Prolia.
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.
Risk minimization measures	Routine risk minimization measures: • None Additional risk minimization measures: • 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.

Jubbonti has been authorised with the condition 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).	22/10/2029

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

In accordance with legal requirements, the current approved UK versions 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 European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

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