OSVYRTI®
(denosumab-desu) injection
60 mg/mL

OSVYRTI® (denosumab-desu): DOSING AND ADMINISTRATION GUIDE

Please see the full Prescribing Information, including Boxed WARNING and Important Safety Information on Pages 11–13.

CONTENTS

OSVYRTI (denosumab-desu): A DENOSUMAB BIOSIMILAR

OSVYRTI IS AN INTERCHANGEABLE DENOSUMAB BIOSIMILAR WITH AN IDENTICAL MECHANISM OF ACTION TO PROLIA® (denosumab), AND FDA-APPROVED FOR THE SAME INDICATIONS[1,2]

INDICATIONS AND USAGE

OSVYRTI is a RANKL inhibitor indicated for treatment:[1]

- of postmenopausal women with osteoporosis at high risk for fracture
- to increase bone mass in men with osteoporosis at high risk for fracture
- of glucocorticoid-induced osteoporosis in men and women at high risk for fracture
- to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer
- to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer

Please see the full Prescribing Information for complete Indications and Usage.

OSVYRTI IS SUPPLIED AS A SINGLE-DOSE PRE-FILLED SYRINGE (60 mg/mL)[1]

FDA, Food and Drug Administration; RANKL, receptor activator of nuclear factor-kappa B ligand.

BOXED WARNING

BOXED WARNING: SEVERE HYPOCALCEMIA IN PATIENTS WITH ADVANCED KIDNEY DISEASE

- **Patients with advanced chronic kidney disease are at greater risk of severe hypocalcemia following denosumab products administration. Severe hypocalcemia resulting in hospitalization, life-threatening events and fatal cases have been reported.**
- **The presence of chronic kidney disease-mineral bone disorder (CKD-MBD) markedly increases the risk of hypocalcemia.**
- **Prior to initiating OSVYRTI in patients with advanced chronic kidney disease, evaluate for the presence of CKD-MBD. Treatment with OSVYRTI in these patients should be supervised by a healthcare provider with expertise in the diagnosis and management of CKD-MBD.**

Please see the full Important Safety Information on pages 11–13 and full Prescribing Information.

STARTING YOUR PATIENTS ON OSVYRTI

Before initiating treatment with OSVYRTI, ensure the following evaluations are complete:[1]

- **PREGNANCY TESTING**
  Pregnancy must be ruled out. Perform pregnancy testing in all females of reproductive potential prior to administration of OSVYRTI
- **LABORATORY TESTING IN PATIENTS WITH ADVANCED CHRONIC KIDNEY DISEASE**
  In patients with advanced chronic kidney disease [i.e., eGFR <30 mL/min/1.73 m^2], including dialysis-dependent patients, evaluate for the presence of CKD-MBD with iPTH, serum calcium, 25(OH) vitamin D, and 1,25 $(OH)_2$ vitamin D

  Consider also assessing bone turnover status (serum markers of bone turnover or bone biopsy) to evaluate the underlying bone disease that may be present.


Actor portrayal.

CKD-MBD, chronic kidney disease-mineral and bone disorder; eGFR, estimated glomerular filtration rate; iPTH, intact parathyroid hormone.

SELECT IMPORTANT SAFETY INFORMATION

Contraindications: OSVYRTI is contraindicated in patients with hypocalcemia. Pre-existing hypocalcemia must be corrected prior to initiating OSVYRTI. OSVYRTI is contraindicated in women who are pregnant and may cause fetal harm. In women of reproductive potential, pregnancy testing should be performed prior to initiating treatment. OSVYRTI is contraindicated in patients with hypersensitivity to denosumab products. Reactions have included anaphylaxis, facial swelling and urticaria.

Please see the full Important Safety Information on pages 11–13 and full Prescribing Information.

DOSING SCHEDULE

DOSING AND ADMINISTRATION OF OSVYRTI IS THE SAME AS PROLIA[1,2]

THE RECOMMENDED DOSE IS[1]

one pre-filled syringe of **60 mg**

administered by a healthcare provider every **6 months**

as a single **subcutaneous** injection in the upper arm, upper thigh, or abdomen

What if my patient misses their dose?

If a dose of OSVYRTI is missed, administer the injection as soon as your patient is available[1]

↓

New baseline date: Schedule next injection 6 months from the date of their last injection[1]

↓

MAINTAIN EVERY 6-MONTH SCHEDULE

All patients should receive **1000 mg of calcium** daily and at least **400 IU of vitamin D** daily.[1]

IU, international unit.

SELECT IMPORTANT SAFETY INFORMATION

Severe Hypocalcemia and Mineral Metabolism Changes: Pre-existing hypocalcemia must be corrected prior to initiating therapy; severe hypocalcemia and fatal cases have been reported with denosumab products. Adequately supplement all patients with calcium and vitamin D.

In patients without advanced CKD who are predisposed to hypocalcemia and disturbances of mineral metabolism, assess serum calcium and mineral levels (phosphorus and magnesium) 10 to 14 days after OSVYRTI injection. In some postmarketing cases, hypocalcemia persisted for weeks or months and required frequent monitoring and intravenous and/or oral calcium replacement, with or without vitamin D.

PATIENTS WITH ADVANCED CHRONIC KIDNEY DISEASE
Patients with advanced chronic kidney disease (eGFR <30 mL/min/1.73 m^2), including dialysis-dependent patients, are at high risk for severe hypocalcemia after denosumab products administration, which can lead to hospitalization, life-threatening events, or death. CKD-MBD and concomitant calcimimetic use further increase risk.

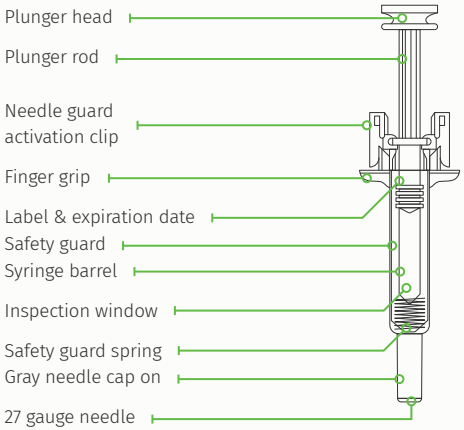
Assess for mineral bone disorder before OSVYRTI treatment, monitor serum calcium weekly for the first month, then monthly, and educate patients on hypocalcemia symptoms and the need for adequate calcium and activated vitamin D supplementation.

Please see the full Important Safety Information on pages 11–13 and full Prescribing Information.

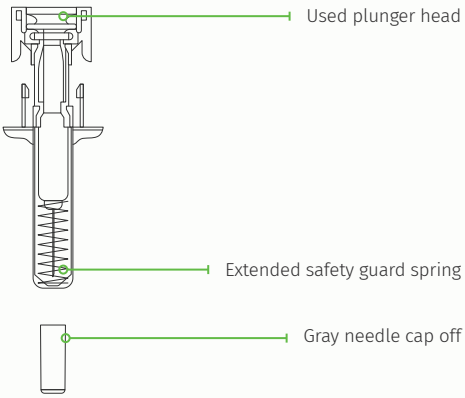
THE OSVYRTI PRE-FILLED SYRINGE

The OSVYRTI single-dose pre-filled syringe comprises features designed to support the injection experience for your patients.[1,3]

BEFORE USE



AFTER USE



The pre-filled syringe is not made with natural rubber latex.

HANDLING TIPS

- In order to minimize accidental needlestick injury, the OSVYRTI pre-filled syringe will have a safety guard that will be activated to cover the needle **after** the injection is given[1]
- **DO NOT** touch the needle guard activation clips before use. Touching them may cause the syringe needle guard to be activated too early[1]
- Grab the safety guard to remove the pre-filled syringe from the tray[1]
- **DO NOT** use the pre-filled syringe if it has been dropped on a hard surface. Use a new pre-filled syringe[1]

SELECT IMPORTANT SAFETY INFORMATION

Same Active Ingredient: Patients receiving OSVYRTI should not receive other denosumab products concomitantly.

Hypersensitivity: Clinically significant hypersensitivity including anaphylaxis has been reported with denosumab products. Symptoms included hypotension, dyspnea, throat tightness, facial and upper airway edema, pruritus and urticaria. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue further use of OSVYRTI.

Please see the full Important Safety Information on pages 11–13 and full Prescribing Information.

PREPARING OSVYRTI FOR ADMINISTRATION

VISUALLY INSPECT FOR PARTICULATE MATTER AND DISCOLORATION.[1]

OSVYRTI is a clear, colorless to pale yellow solution.
DO NOT use if the solution is discolored or cloudy or if the solution contains particles or foreign particulate matter.[1]

CHECK THE EXPIRATION DATE.[1]

DO NOT use OSVYRTI after the expiration date printed on the label.[1]

For more details, refer to **'Storage and Handling'** on page 10.

VISUALLY INSPECT THAT THE NEEDLE GUARD HAS NOT BEEN ACTIVATED.[1]

If the transparent needle guard is covering the needle cover, the needle guard has already been activated. **DO NOT** use the pre-filled syringe if the needle guard is activated. Get another pre-filled syringe that has not been activated and is ready for use.[1]

OSVYRTI MAY BE BROUGHT TO ROOM TEMPERATURE.[1]

Prior to administration, OSVYRTI may be removed from the refrigerator and brought to room temperature up to 25°C (77°F) by standing in the original carton. This generally takes **15 to 30 minutes**.[1]

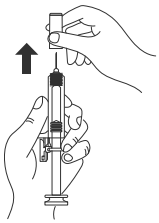
DO NOT warm OSVYRTI in any other way.[1]

ADMINISTERING OSVYRTI

Wash hands thoroughly with soap and warm water prior to administering OSVYRTI.

STEP 1: REMOVE GRAY NEEDLE CAP

Remove the needle cap.



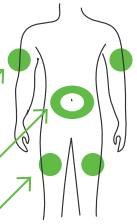
STEP 2: ADMINISTER SUBCUTANEOUS INJECTION

A

Choose an injection site.

The recommended injection sites for OSVYRTI include:

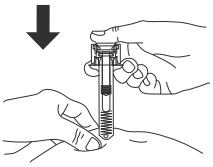
- The upper arm
- The abdomen
- The upper thigh



B

Insert the needle and inject all the liquid subcutaneously.

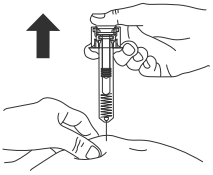
DO NOT administer into a muscle or a blood vessel.



C

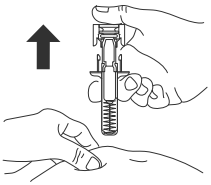
Keep the plunger fully pressed down while you carefully pull the needle straight out from the injection site.

DO NOT put the gray needle cap back on the needle.



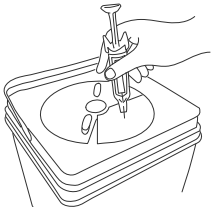
STEP 3: NEEDLE SAFETY GUARD ACTIVATION

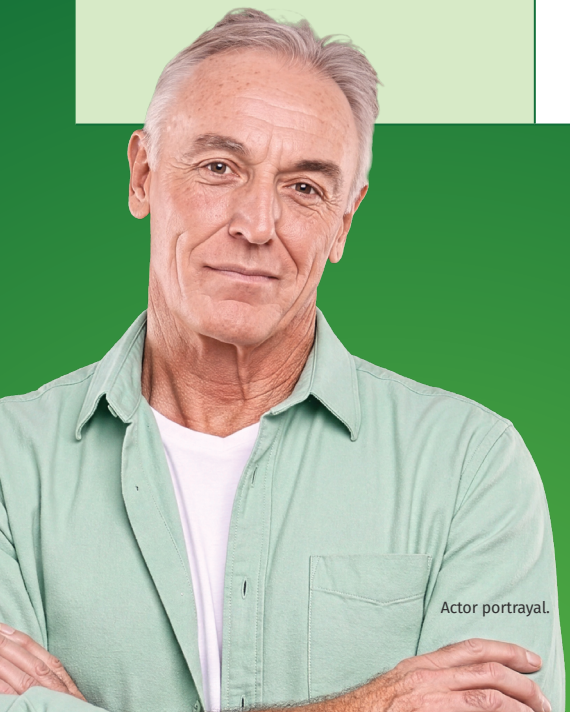
Slowly release the plunger and allow the needle guard to automatically cover the exposed needle.



STEP 4: FINISH

Immediately dispose of the syringe and needle cap in the nearest sharps container. **DO NOT** put the needle cap back on the used syringe.





Actor portrayal.

STORAGE AND HANDLING

	Store OSVYRTI in the original carton in order to protect from light[1]
	Store OSVYRTI refrigerated at 2°C to 8°C (36°F to 46°F). **DO NOT** freeze[1]
	Once removed from the refrigerator, OSVYRTI must not be exposed to temperatures above 25°C (77°F) and must be used within 14 days. If not used within 14 days, OSVYRTI must be discarded. **DO NOT** use OSVYRTI after the expiry date printed on the label[1]
	Protect OSVYRTI from direct light and heat[1]
	Avoid vigorous shaking of OSVYRTI[1]

IMPORTANT SAFETY INFORMATION

BOXED WARNING: SEVERE HYPOCALCEMIA IN PATIENTS WITH ADVANCED KIDNEY DISEASE

See full prescribing information for complete boxed warning.

- **Patients with advanced chronic kidney disease are at greater risk of severe hypocalcemia following denosumab products administration. Severe hypocalcemia resulting in hospitalization, life-threatening events and fatal cases have been reported.**
- **The presence of chronic kidney disease-mineral bone disorder (CKD-MBD) markedly increases the risk of hypocalcemia.**
- **Prior to initiating OSVYRTI in patients with advanced chronic kidney disease, evaluate for the presence of CKD-MBD. Treatment with OSVYRTI in these patients should be supervised by a healthcare provider with expertise in the diagnosis and management of CKD-MBD.**

Contraindications: OSVYRTI is contraindicated in patients with hypocalcemia. Pre-existing hypocalcemia must be corrected prior to initiating OSVYRTI. OSVYRTI is contraindicated in women who are pregnant and may cause fetal harm. In women of reproductive potential, pregnancy testing should be performed prior to initiating treatment. OSVYRTI is contraindicated in patients with hypersensitivity to denosumab products. Reactions have included anaphylaxis, facial swelling and urticaria.

Severe Hypocalcemia and Mineral Metabolism Changes: Pre-existing hypocalcemia must be corrected prior to initiating therapy; severe hypocalcemia and fatal cases have been reported with denosumab products. Adequately supplement all patients with calcium and vitamin D.

In patients without advanced CKD who are predisposed to hypocalcemia and disturbances of mineral metabolism, assess serum calcium and mineral levels (phosphorus and magnesium) 10 to 14 days after OSVYRTI injection. In some postmarketing cases, hypocalcemia persisted for weeks or months and required frequent monitoring and intravenous and/or oral calcium replacement, with or without vitamin D.

Patients with Advanced Chronic Kidney Disease
Patients with advanced chronic kidney disease (eGFR <30 mL/min/1.73 m^2), including dialysis-dependent patients, are at high risk for severe hypocalcemia after denosumab products administration, which can lead to hospitalization, life-threatening events, or death. CKD-MBD and concomitant calcimimetic use further increase risk.

Assess for mineral bone disorder before OSVYRTI treatment, monitor serum calcium weekly for the first month, then monthly, and educate patients on hypocalcemia symptoms and the need for adequate calcium and activated vitamin D supplementation.

Same Active Ingredient: Patients receiving OSVYRTI should not receive other denosumab products concomitantly.

Hypersensitivity: Clinically significant hypersensitivity including anaphylaxis has been reported with denosumab products. Symptoms included hypotension, dyspnea, throat tightness, facial and upper airway edema, pruritus and urticaria. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue further use of OSVYRTI.

Osteonecrosis of the Jaw (ONJ): ONJ, which can occur spontaneously, is generally associated with tooth extraction and/or local infection with delayed healing and has been reported in patients receiving denosumab products. An oral exam should be performed prior to initiation of OSVYRTI. Concomitant administration of drugs associated with ONJ may increase the risk of developing ONJ. The risk of ONJ may increase with duration of exposure to denosumab products.

For patients requiring invasive dental procedures, clinical judgment should guide the management plan based on individual benefit-risk assessment.

Patients suspected of having or who develop ONJ should receive care by a dentist or an oral surgeon. Extensive dental surgery to treat ONJ may exacerbate the condition. Discontinuation of OSVYRTI should be considered based on individual benefit-risk assessment.

Atypical Subtrochanteric and Diaphyseal Femoral Fractures: Atypical low-energy, or low trauma fractures of the shaft have been reported with denosumab products. These fractures can occur anywhere in the femoral shaft from just below the lesser trochanter to above the supracondylar flare and are transverse or short oblique in orientation without evidence of comminution. Causality has not been established as these fractures also occur in osteoporotic patients who have not been treated with antiresorptive agents.

Atypical femoral fractures most commonly occur with minimal or no trauma to the affected area. They may be bilateral, and many patients report prodromal pain in the affected area, usually presenting as dull, aching thigh pain, weeks to months before a complete fracture occurs. A number of reports note that patients were also receiving treatment with glucocorticoids (e.g. prednisone) at the time of fracture.

During OSVYRTI treatment, advise patients to report new or unusual thigh, hip, or groin pain. Any patient who presents with thigh or groin pain should be evaluated to rule out an incomplete femur fracture. Patients presenting with an atypical femur fracture should also be assessed for symptoms and signs of fracture in the contralateral limb. Interruption of OSVYRTI therapy should be considered, pending a risk/benefit assessment, on an individual basis.

Multiple Vertebral Fractures Following Discontinuation of Treatment: Following discontinuation of denosumab treatment, fracture risk increases, including the risk of multiple vertebral fractures.

New vertebral fractures occurred as early as 7 months (on average 19 months) after the last dose of denosumab. Prior vertebral fracture was a predictor of multiple vertebral fractures after denosumab discontinuation. Evaluate an individual's benefit/risk before initiating treatment with OSVYRTI. If OSVYRTI treatment is discontinued, patients should be transitioned to an alternative antiresorptive therapy.

Serious Infections: Serious infections leading to hospitalization were reported more frequently in patients taking denosumab. Serious skin infections, and infections of the abdomen, urinary tract and ear were more frequent in patients treated with denosumab.

Endocarditis was also reported more frequently in denosumab-treated patients. Advise patients to seek prompt medical attention if they develop signs or symptoms of severe infection, including cellulitis.

Patients on concomitant immunosuppressant agents or with impaired immune systems may be at increased risk for serious infections. In patients who develop serious infections while on OSVYRTI, prescribers should assess the need for continued therapy.

Dermatologic Adverse Reactions: Epidermal and dermal adverse events such as dermatitis, eczema and rashes occurred at a significantly higher rate in patients taking denosumab. Most of these events were not specific to the injection site. Consider discontinuing OSVYRTI if severe symptoms develop.

Musculoskeletal Pain: Severe and occasionally incapacitating bone, joint, and/or muscle pain has been reported with denosumab products. Consider discontinuing OSVYRTI use if severe symptoms develop.

Suppression of Bone Turnover: Treatment with denosumab resulted in significant suppression of bone remodeling as evidenced by markers of bone turnover and bone histomorphometry. The significance and effect of long-term treatment with denosumab products are unknown. Monitor patients for consequences, including ONJ, atypical fractures, and delayed fracture healing.

Hypercalcemia in Pediatric Patients with Osteogenesis Imperfecta: OSVYRTI is not approved for use in pediatric patients. Hypercalcemia has been reported in pediatric patients with osteogenesis imperfecta treated with denosumab products. Some cases required hospitalization.

Most Common Adverse Reactions:

- **Postmenopausal osteoporosis:** Greater than 5% and more common than placebo: back pain, pain in extremity, hypercholesterolemia, musculoskeletal pain, and cystitis. Pancreatitis has been reported in clinical trials.
- **Male osteoporosis:** Greater than 5% and more common than placebo: back pain, arthralgia, and nasopharyngitis.
- **Glucocorticoid-induced osteoporosis:** Greater than 3% and more common than active-control group were: back pain, hypertension, bronchitis, and headache.
- **Bone loss due to hormone ablation for cancer:** Greater than or equal to 10% and more common than placebo: arthralgia and back pain. Pain in extremity and musculoskeletal pain have also been reported in clinical trials.

INDICATIONS

OSVYRTI is a RANK ligand (RANKL) inhibitor indicated for treatment:

- of postmenopausal women with osteoporosis at high risk for fracture
- to increase bone mass in men with osteoporosis at high risk for fracture
- of glucocorticoid-induced osteoporosis in men and women at high risk for fracture
- to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer
- to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer

To report SUSPECTED ADVERSE REACTIONS, contact Accord BioPharma Inc at 1-866-941-7875 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

OSVYRTI (denosumab-desu) injection is supplied in a 60 mg/mL single-dose pre-filled syringe.

For more information, see the full Prescribing Information, including Boxed Warning or go to www.osvyrtihcp.com.

NOTES

Actor portrayal.

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(denosumab-desu) injection
60 mg/mL

REFERENCES

1. OSVYRTI Prescribing Information. Accord BioPharma.

2. PROLIA Prescribing Information. Amgen Inc.

3. Accord Data on File.

HCR-OSV-2600002