Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) – 1986

This medicine is dispensed with a doctor's prescription only

Jubbonti®

Solution for subcutaneous injection

Active ingredient:
Each pre-filled syringe contains:
denosumab 60 mg in 1 ml solution

Inactive ingredients and allergens in this medicine: See section 2 under 'Important information about some ingredients of the medicine', and section 6 'Additional information'.

Read the entire leaflet carefully before using the medicine.
This leaflet contains concise information about the medicine. If you have any other questions, refer to the doctor or pharmacist.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.

In addition to this leaflet, Jubbonti also has a patient safety information card. This card includes important safety information that you should know before treatment initiation and during the treatment with Jubbonti and act according to it. Carefully read the patient safety information card and the patient leaflet before using this medicine. The card should be kept for additional reading as needed.

Jubbonti is a biosimilar medicine. For additional information about biosimilars, refer to the Ministry of health website:
https://www.gov.il/he/Departments/General/biosimilar

1. What is the medicine intended for?

Jubbonti is not intended for use in children and adolescents under 18 years old.

Jubbonti is used to treat:
- osteoporosis in women after the menopause (postmenopausal) and men who have an increased risk of fractures (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 due to long-term systemic glucocorticoids therapy of a daily dosage equivalent to 7.5 mg or greater of prednisone and expected to remain on glucocorticoids for at least 3 months, in adult patients at high risk of fracture.

Therapeutic group: Medicines for the treatment of bone disease - other medicines affecting bone structure and mineralization.

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. Estrogen helps keep bones healthy. After the menopause, estrogen 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 estrogen 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.

2. Before using the medicine

Do not use the medicine if:

- you have low calcium levels in the blood (hypocalcemia).
- you are sensitive (allergic) to denosumab or to any of the additional ingredients contained in the medicine (see section 6 'Additional information').

Special warnings regarding the use of the medicine
Talk to your doctor or pharmacist before using Jubbonti.

While being treated with Jubbonti, you may develop a skin infection with symptoms such as a swollen, red area of skin, most commonly in the lower leg, that feels tender and hot (cellulitis), and possibly accompanied by symptoms of fever. Please tell your doctor immediately if you develop any of these symptoms.

You should also take vitamin D and calcium supplements during treatment with Jubbonti. Your doctor will discuss this with you.

You may have low levels of calcium in your blood while receiving Jubbonti. Please tell your doctor immediately if you notice any of the following symptoms: spasms, twitches, or cramps in your muscle, and/or numbness or tingling in your fingers, toes or around your mouth, and/or fits (seizures), confusion, or loss of consciousness.

Severe low blood calcium levels leading to hospitalization and even life-threatening reactions have been reported in rare cases. Therefore, before each dose and in patients predisposed to hypocalcemia within the first two weeks after the initial dose, the calcium levels in your blood will be checked (via blood test).

Tell your doctor if you have or have ever had severe kidney problems, kidney failure or have needed dialysis or are taking medicines called glucocorticoids (such as prednisolone or dexamethasone), which may increase your risk of having low blood calcium levels if you do not take calcium supplements.

Problems with your mouth, teeth or jaw
A side effect called osteonecrosis of the jaw (ONJ) (bone damage in the jaw) has been reported rarely (may affect up to 1 in 1,000 people) in patients receiving denosumab for osteoporosis. The risk of ONJ increases in patients treated for a long time (may affect up to 1 in 200 people if treated for 10 years). ONJ can also occur after stopping treatment. It is important to try to prevent ONJ developing as it may be a painful condition that can be difficult to treat. In order to reduce the risk of developing ONJ, take the following precautions:

Before receiving treatment, tell your doctor or nurse (healthcare team) if:
- you have any problems with your mouth or teeth such as poor dental health, gum disease, or a planned tooth extraction.
- you do not receive routine dental care or have not had a dental check-up for a long time.
- you are a smoker (as this may increase the risk of dental problems).
- you have recently been treated with a bisphosphonate (used to treat or prevent bone problems).
- you are taking medicines called corticosteroids (such as prednisolone or dexamethasone).
- you have cancer.

Your doctor may ask you to undergo a dental examination before you start treatment with Jubbonti.
While being treated, you should make sure to maintain good oral hygiene and have routine dental check-ups. If you wear dentures you should make sure these fit properly. If you are under dental treatment or will undergo dental surgery (e.g. tooth extractions), inform your doctor about your dental treatment and tell your dentist that you are being treated with Jubbonti.

Contact your doctor and dentist immediately if you experience any problems with your mouth or teeth such as loose teeth, pain or swelling, or non-healing of sores or discharge, as these could be signs of ONJ.

Unusual thigh bone fractures
Some people have developed unusual fractures in their thigh bone while being treated with Jubbonti. Contact your doctor if you experience new or unusual pain in your hip, groin, or thigh.

Children and adolescents
Jubbonti is not intended for use in children and adolescents under 18 years of age.

Interactions with other medicines
If you are taking, have recently taken or might take any other medicines including non-prescription medicines and food supplements, tell the doctor or the pharmacist. Particularly if you are taking:
- another medicine containing denosumab

You should not take Jubbonti together with other medicines containing denosumab.

Pregnancy and breastfeeding
Denosumab has not been tested in pregnant women. It is important to tell your doctor if you are pregnant, think you may be pregnant or are planning to get pregnant. Jubbonti is not recommended for use if you are pregnant. Women of child-bearing potential should use effective methods of contraception during treatment with Jubbonti and for at least 5 months after stopping treatment with Jubbonti.

If you become pregnant during treatment with Jubbonti or less than 5 months after stopping treatment with Jubbonti, please inform your doctor.

It is not known whether denosumab is excreted in breast milk. It is important to tell your doctor if you are breastfeeding or plan to do so. Your doctor will then help you decide whether to stop breastfeeding, or whether to stop taking Jubbonti, considering the benefit of breastfeeding to the baby and the benefit of Jubbonti to the mother.

If you are breastfeeding during Jubbonti treatment, please inform your doctor.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines
Jubbonti has no or negligible influence on the ability to drive and use machines.

Important information about some ingredients of the medicine

Jubbonti contains sorbitol
This medicine contains 47 mg sorbitol in each ml of solution.

Jubbonti contains polysorbate
This medicine contains 0.1 mg polysorbate 20 in each ml of solution.
Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

Jubbonti contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per 60 mg (1 ml solution), that is to say essentially 'sodium-free'.

3. How should you use the medicine?

Always use this medicine according to your doctor's instructions.
You should check with the doctor or the pharmacist if you are not sure about the dosage and treatment regimen.
The dosage and treatment regimen will be determined by your doctor only.

The recommended dosage is 60 mg administered once every 6 months, as a single injection under the skin (subcutaneous) using one pre-filled syringe.

The best areas to inject are the top of your thighs and the abdomen. Your carer can also inject into the outer area of your upper arm.

Please consult your doctor on a possible date for the next injection. The Jubbonti patient information leaflet contains a reminder card that can be removed and used to document the date of your next injection.

You should also take vitamin D and calcium supplements while you are receiving treatment with Jubbonti. Your doctor will discuss this with you.

Your doctor may decide that it is best for you or your carer to inject Jubbonti. Your doctor or healthcare provider will show you or your carer how to use Jubbonti. For instructions on how to inject Jubbonti, please read the section at the end of this leaflet.

Do not exceed the recommended dose.
Jubbonti should be administered under the responsibility of a healthcare professional.

If you accidentally have taken a higher dosage
If you have taken an overdose, or if a child has accidentally swallowed the medicine, refer immediately to a doctor or to a hospital emergency room and bring the package of medicine with you.

If you forget to take the medicine
If a dose of Jubbonti is missed, the injection should be received as soon as possible. Thereafter, injections should be scheduled every 6 months from the date of the last injection.

Adhere to the treatment as recommended by the doctor.

If you stop taking Jubbonti
To get the most benefit from your treatment in reducing the risk of fractures, it is important to use Jubbonti for as long as your doctor prescribes it. Do not stop your treatment without contacting your doctor.

Stopping use of Jubbonti can increase the risk of broken bones in the spine, especially in patients with a background of broken bones in the spine. Do not stop taking Jubbonti without first talking with your doctor. If your Jubbonti treatment is stopped, discuss other available treatment options with your doctor.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Side effects

As with any medicine, use of Jubbonti may cause side effects in some of the users. Do not be alarmed by reading the list of side effects. You may not experience any of them.

Uncommonly, patients receiving Jubbonti may develop skin infections [predominantly inflammation of tissue beneath the skin (cellulitis)]. **Please contact your doctor immediately** if you develop any of these symptoms while receiving treatment with Jubbonti: swollen, red area of skin, usually in the lower leg, that feels tender and hot, and possibly accompanied by symptoms of fever.

Rarely, patients receiving Jubbonti may develop pain in the mouth and/or jaw, swelling or non-healing of sores in the mouth or jaw, discharge, numbness or a feeling of heaviness in the jaw, or loosening of a tooth. These could be signs of bone damage in the jaw (osteonecrosis). **Contact your doctor and dentist immediately** if you experience such symptoms while being treated with Jubbonti or after stopping treatment.

Rarely, patients receiving Jubbonti may have low calcium levels in the blood (hypocalcemia); severely low blood calcium levels may lead to hospitalization and may even be life-threatening. The symptoms include spasms, twitches, or cramps in your muscles, and/or numbness or tingling in your fingers, toes or around your mouth and/or seizures, confusion, or loss of consciousness. If any of these apply to you, **contact your doctor immediately**. Low calcium in the blood may also lead to a change in heart rhythm called QT prolongation which is seen by electrocardiogram (ECG).

Rarely unusual fractures of the thigh bone may occur in patients receiving Jubbonti. **Contact your doctor** if you experience new or unusual pain in your hip, groin or thigh as this may be an early indication of a possible fracture of the thigh bone.

Rarely, allergic reactions may occur in patients receiving Jubbonti. The symptoms include swelling of the face, lips, tongue, throat or other parts of the body; rash, itching or hives (itchy bumps) on the skin, wheezing or difficulty breathing. **Please tell your doctor** if you develop any of these symptoms during treatment with Jubbonti.

Very common side effects (may affect more than 1 in 10 people):
- bone, joint, and/or muscle pain which is sometimes severe,
- arm or leg pain (pain in extremities).

Common side effects (may affect up to 1 in 10 people):
- painful urination, frequent urination, blood in the urine, inability to hold your urine,
- upper respiratory tract infection,
- pain, tingling or numbness that moves down your leg (sciatica),
- constipation,
- abdominal discomfort,
- rash,
- skin condition including itching, redness and/or dryness (eczema),
- hair loss (alopecia).

Uncommon side effects (may affect up to 1 in 100 people):
- fever, vomiting and abdominal discomfort or pain (diverticulitis, inflammation of the intestine),
- ear infection,
- rash that may occur on the skin or sores in the mouth (lichenoid drug eruptions),
- broken bones in the spine after stopping Jubbonti (multiple vertebral fractures).

Very rare side effects (may affect up to 1 in 10,000 people):
- allergic reaction that can damage blood vessels mainly in the skin (e.g. purple or brownish-red spots, hives or skin sores) (hypersensitivity vasculitis).

Side effects of unknown frequency (the frequency of these effects has not been established yet):
- Talk to your doctor if you have ear pain, discharge from the ear and/or an ear infection. These could be signs of bone damage in the ear,
- severe allergic reaction (drug reaction with eosinophilia and systemic symptoms [DRESS] syndrome) with skin rash/blisters, fever and/or increase in a type of white blood cell (eosinophils) with possible organ damage, such as liver, kidney, or lung.

If a side effect has appeared, if any of the side effects get worse or when you suffer from a side effect that has not been mentioned in this leaflet, you should consult the doctor.

Reporting of side effects
Side effects can be reported to the Ministry of Health by clicking on the link "Reporting of Side Effects due to Medical Treatment" located on the Ministry of Health homepage (www.health.gov.il) which directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

5. How to store the medicine?

Avoid poisoning! This medicine and any other medicine should be kept in a closed place out of the sight and reach of children and/or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.
Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines that are no longer required. These measures will help to protect the environment.

Storage conditions:
Store in a refrigerator (2°C-8°C).
Do not freeze.
Do not shake.

Keep in the outer carton in order to protect from light.
The package with the pre-filled syringe may be left outside the refrigerator to reach room temperature (up to 25°C) before injection. This will make the injection more comfortable. Once your pre-filled syringe has been left outside the refrigerator to reach room temperature (up to 25°C), it must be used within 30 days.

6. Additional information

In addition to the active ingredient, the medicine also contains:
sorbitol, acetic acid glacial, polysorbate 20, sodium hydroxide, hydrochloric acid and water for injections

What does the medicine look like and what is the content of the package:
A pre-filled syringe with a clear to slightly opalescent colourless to slightly yellowish or slightly brownish sterile solution for injection.
A package of Jubbonti contains one pre-filled syringe with a needle guard.

License Holder and Importer's name and address:
Sandoz Pharmaceuticals Israel Ltd., P.O.Box 9015, Tel Aviv, Israel.

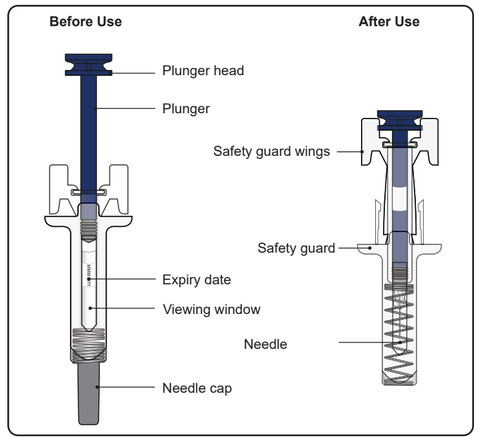
Revised in February 2025.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 178-84-38243-00

Instructions for Use
These "Instructions for Use" contain information on how to inject Jubbonti.

If your doctor decides that you or your caregiver may be able to give your injections of Jubbonti at home, ensure that your doctor or nurse shows you or your caregiver how to prepare and inject with the Jubbonti pre-filled syringe before you use it for the first time.

Be sure that you read and understand these Instructions for Use before injecting with the Jubbonti pre-filled syringe. Talk to your doctor if you have any questions.



Important information you need to know before injecting Jubbonti

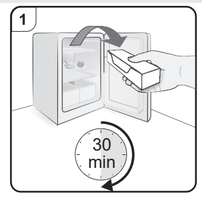
- Jubbonti is for subcutaneous injection only (inject directly into fatty layer under the skin).
- **Do not** use the pre-filled syringe if any of the safety seals on the outer carton or the seal of the plastic tray is broken.
- **Do not** shake the pre-filled syringe at any time.
- **Do not** use if the pre-filled syringe has been dropped onto a hard surface or dropped after removing the needle cap.
- The pre-filled syringe has a safety guard that activates to cover the needle after the injection is finished. The safety guard helps to prevent needle stick injuries to anyone who handles the pre-filled syringe after injection.
- **Be careful not to touch the safety guard wings** before use. Touching them may cause the safety guard to activate too early.
- **Do not** attempt to re-use or disassemble the pre-filled syringe.
- **Do not** pull back on the plunger.

Store Jubbonti

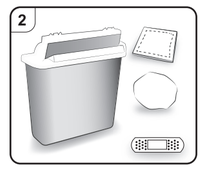
- Store in a refrigerator between 2°C and 8°C.
- **Do not** freeze.
- If needed, you may store the pre-filled syringe at room temperature up to 25°C for up to 30 days.
- Throw away the pre-filled syringe that has been stored at room temperature after 30 days.
- Keep the pre-filled syringe in the original carton until ready to use in order to protect from light.
- Keep out of sight and reach of children.

Prepare to inject Jubbonti

Step 1. Bring to room temperature
Take the carton containing the pre-filled syringe out of the refrigerator and leave it unopened for about 15 to 30 minutes so that it reaches room temperature.

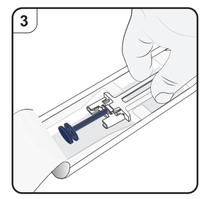


Step 2. Gather supplies
Ensure that you have the following (not included in the carton):
- Alcohol wipe
- Cotton ball or gauze pad
- Sharps disposal container
- Adhesive plaster (bandage)



Step 3. Unpack
Open the plastic tray by peeling away the cover. Remove the pre-filled syringe by holding it in the middle as shown.

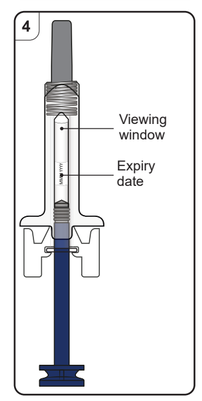
Do not remove the needle cap until you are ready to inject.



Step 4. Perform safety checks
Look through the viewing window of the pre-filled syringe. The liquid inside should be a clear to slightly opalescent, colourless to slightly yellowish or slightly brownish solution. You may see air bubbles in the liquid, which is normal.

Do not attempt to remove the air.
- **Do not** use the pre-filled syringe if liquid is cloudy or contains visible particles.
- **Do not** use the pre-filled syringe if it appears to be damaged or if it has leaked.
- **Do not** use the pre-filled syringe after the expiry date (exp. date), which is printed on the pre-filled syringe label and carton.

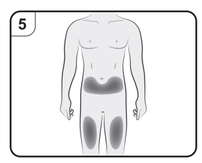
In all of these cases, contact your doctor, nurse or pharmacist.



Step 5. Choose injection site
You should inject into the front of the thighs or the lower stomach area **but not** the area 5 cm around the belly button.

Do not inject into skin that is tender, bruised, red, scaly, hard or into areas with scars or stretch marks.

If your caregiver, doctor or nurse is giving you the injection, they may also inject into the upper arm.

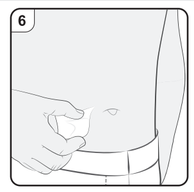


Inject with Jubbonti

Step 6. Clean injection site
Wash your hands with soap and water.

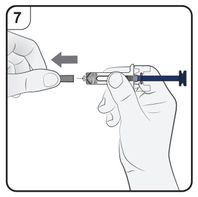
Clean the chosen injection site with an alcohol wipe. Leave it to dry before injecting.

Do not touch or blow on the cleaned area before injecting.



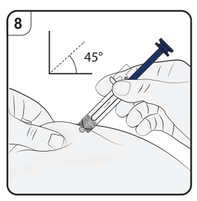
Step 7. Remove needle cap
Firmly pull straight to remove the needle cap from the pre-filled syringe. You may see a drop of liquid at the end of the needle. This is normal.

Do not put the needle cap back on. Throw away the needle cap.

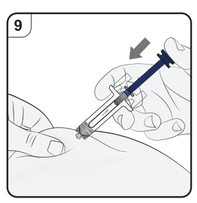


Step 8. Insert needle
Gently pinch the skin at the injection site and hold the pinch throughout the injection. With the other hand insert the needle into the skin at an angle of approximately 45 degrees as shown.

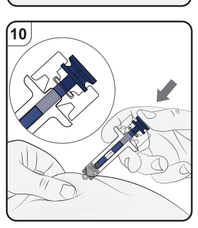
Do not press the plunger while inserting the needle.



Step 9. Start injection
Continue to pinch the skin. Slowly press the plunger **as far as it will go.** This will ensure that a full dose is injected.



Step 10. Complete injection
Confirm that the plunger head is between the safety guard wings as shown. This will ensure that the safety guard has been activated and will cover the needle after the injection is finished.

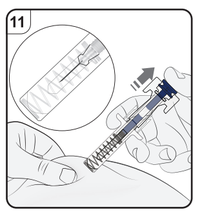


Step 11. Release plunger
Keeping the pre-filled syringe at the injection site, slowly release the plunger until the needle is covered by the safety guard.

Remove the pre-filled syringe from the injection site and release the pinch.

There may be a small amount of blood at the injection site. You can press a cotton ball or gauze pad over the injection site until any bleeding stops.

Do not rub the injection site. If needed, cover the injection site with a small adhesive plaster (bandage).



After the injection

Step 12. Dispose of the pre-filled syringe
Put the pre-filled syringe in a sharps disposal container immediately after use. **Do not** throw away the pre-filled syringe into household waste.

Talk to your doctor or pharmacist about proper disposal of the sharps disposal container. There may be local regulations for disposal.