

Psoriatic arthritis, Ankylosing spondylitis and Psoriasis

Your doctor will start the treatment with two doses of Remsima 100 mg I.V. intravenous infusions at a dosage of 5 mg per kg body weight (given into your vein, usually in your arm, for two hours).

They are administered two weeks apart via intravenous infusion. After 4 weeks from the last intravenous infusion, you will be given Remsima 120 mg/ml S.C. via injection under the skin (subcutaneous injection).

The usual recommended dosage of Remsima 120 mg/ml S.C. subcutaneous injection is 120 mg once every two weeks, regardless of body weight.

Crohn’s disease and ulcerative colitis

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The usual recommended dosage of Remsima 120 mg/ml S.C. subcutaneous injection is 120 mg once every two weeks, regardless of body weight.

Do not exceed the recommended dose.

How Remsima 120 mg/ml S.C. is given

- Remsima 120 mg/ml S.C. solution for injection is administered by injection under the skin (subcutaneous use) only. It is important to check the product labels to ensure that the correct formulation is being given as prescribed.

- The initial two intravenous infusions will be given to you by your physician or nurse.
- After the first two initial intravenous infusions of Remsima 100 mg I.V., the first dose of Remsima 120 mg/ml S.C. will be administered after receiving a training from your physician or nurse.
- After proper training, if you feel that you are well-trained and confident to inject Remsima 120 mg/ml S.C. yourself, you may inject the subsequent doses of Remsima 120 mg/ml S.C. yourself at home.
- Talk to your physician if you have any questions about giving yourself an injection. You will find detailed “Instructions for use” at the end of this leaflet.

If you have accidentally used a higher dosage of Remsima 120 mg/ml S.C.

If you have used a higher dosage of Remsima 120 mg/ml S.C. (either by injecting too much on a single occasion or by using it too frequently), talk to the physician, pharmacist or nurse immediately.

It is important that the outer carton of the medicine will be with you, even if it is empty.

If you forgot to use Remsima 120 mg/ml S.C.

A forgotten dose up to 7 days

If you forgot to inject Remsima 120 mg/ml S.C. for up to 7 days, after the original scheduled date of receiving the dose, inject the missed dose immediately. Take your next dose on the next originally planned date, and thereafter every two weeks.

A forgotten dose for 8 days and more

If you forgot to inject Remsima 120 mg/ml S.C. for 8 days and more, after the original scheduled date of receiving the dose, you should not inject the forgotten dose. Take your next dose on the next originally planned date, and thereafter every 2 weeks.

If you are not sure when to inject Remsima 120 mg/ml S.C., contact your physician.

Continue with the treatment as recommended by the physician.

Even if there is an improvement in your health, do not stop the treatment with this medicine without consulting the physician.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.

If you have further questions on the use of this medicine, consult the physician or pharmacist.

4. SIDE EFFECTS

As with any medicine, the use of Remsima 120 mg/ml S.C. may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Most side effects are mild to moderate. However, some side effects may be serious and require treatment. Side effects may also occur after your treatment with Remsima 120 mg/ml S.C. has stopped.

Contact your physician immediately if you notice any of the following signs:

- Signs of an allergic reaction**, such as swelling of the face, lips, mouth or throat which may cause difficulty in swallowing or breathing, skin rash, hives, swelling of the hands, feet or ankles. Some of these reactions may be serious or life-threatening. An allergic reaction could happen within 2 hours of your injection or later. More signs of allergic side effects that may happen up to 12 days after your injection include pain in the muscles, fever, joint or jaw pain, sore throat or headache.
- Signs of a local injection site reaction**, such as redness, pain, itching, swelling, hardness, bruising, bleeding, cold sensation, tingling sensation, irritation, rash, ulcer, hives, blisters and scab.
- Signs of heart problems**, such as chest discomfort or pain, arm pain, stomach pain, shortness of breath, anxiety, lightheadedness, dizziness, fainting, sweating, nausea, vomiting, fluttering or pounding in your chest, a fast or a slow heartbeat and swelling of your feet.
- Signs of infection (including tuberculosis)**, such as fever, feeling tired, cough which may be persistent, shortness of breath, flu-like symptoms, weight loss, night sweats, diarrhea, wounds, accumulation of pus in the gut or around the anus (abscess), dental problems or burning sensation when urinating.
- Possible signs of cancer** including but not limited to swelling of lymph nodes, weight loss, fever, unusual skin nodules, changes in moles or skin coloring, or unusual vaginal bleeding.
- Signs of lung problems**, such as coughing, breathing difficulties or tightness in the chest.

- Signs of nervous system problems (including eye problems)**, such as signs of a stroke (sudden numbness or weakness of your face, arms or legs, especially on one side of your body; sudden confusion, trouble speaking or understanding; trouble seeing in one or both eyes, trouble walking, dizziness, loss of balance or coordination or a severe headache), fits, tingling or numbness in different parts of your body or weakness in the arms or legs, changes in eyesight, such as double vision or other eye problems.

- Signs of liver problems** (including hepatitis B infection when you have had hepatitis B in the past), such as yellowing of the skin or the eyes, dark brown-colored urine, pain or swelling in the upper right side of the stomach area, joint pain, skin rash, or fever.

- Signs of an immune system disorder called lupus**, such as joint pain or a rash on cheeks or arms that is sensitive to the sun (lupus) or cough, shortness of breath, fever or skin rash (sarcoidosis).

- Signs of low blood counts**, such as persistent fever, bleeding or bruising more easily, small red or purple spots caused by bleeding under the skin or looking pale.
- Signs of serious skin problems**, such as reddish target-like spots or circular patches often with central blisters on the trunk, large areas of peeling and shedding (exfoliating) skin, ulcers: in the mouth, throat, nose, genitals and eyes, or small pus-filled bumps that can spread over the body. These skin reactions can be accompanied by fever.

Tell your physician straight away if you notice any of the side effects listed above.

The following side effects have been observed with Remsima 120 mg/ml S.C.:

Very common side effects: may appear in more than 1 out of 10 users

- Stomach pain, nausea
- Viral infection, such as herpes or flu
- Upper respiratory infection, such as sinusitis
- Headache
- Side effects due to the injection
- Pain

Common side effects: may appear in up to 1 out of 10 users

- Changes in liver function, increase in liver enzymes (diagnosed in blood test)
- Lung or chest infections, such as bronchitis or pneumonia
- Difficulty breathing or painful breathing, chest pain
- Bleeding in the stomach or intestines, diarrhea, indigestion, heartburn, constipation
- Hives (nettle-type rash), itchy rash or dry skin
- Balance problems or feeling dizzy
- Fever, increased sweating
- Blood circulation problems, such as low or high blood pressure
- Bruising, hot flush or nosebleed, warm and red skin (flushing)
- Feeling tired or weak
- Bacterial infections, such as blood poisoning, abscess or infection of the skin (cellulitis)
- Infection of the skin due to a fungus

- Blood problems, such as anemia or low white blood cell count
- Swollen lymph nodes
- Depression, problems sleeping
- Eyes problems, including red eyes and infections
- Fast heart beat (tachycardia) or palpitations
- Pain in the joints, muscles or back
- Urinary tract infection

- Psoriasis, skin problems, such as eczema and hair loss
- Reactions at the injection site, such as pain, swelling, redness and itching
- Chills, a build-up of fluid under the skin which causing swelling
- Feeling numb or tingling

Uncommon side effects: may appear in up to 1 out of 100 users

- Shortage of blood supply, swelling of a vein
- Accumulation of blood outside the blood vessels (hematoma) or bruising
- Skin problems, such as blistering, warts, abnormal skin coloration or pigmentation, or swollen lips, or thickening of the skin, or red, scaly and flaky skin
- Severe allergic reactions (such as anaphylaxis), an immune system disorder called lupus, allergic reactions to foreign proteins
- Longer healing time of wounds
- Swelling of the liver (hepatitis) or gall bladder, liver damage
- Feeling forgetful, irritable, confused, nervous
- Eye problems including blurred or reduced vision, puffy eyes or sty
- New heart failure or worsening of existing heart failure, slow heart rate
- Fainting
- Convulsions, nerve problems
- A hole in the bowel or blockage of the intestines, stomach pain or cramps
- Swelling of the pancreas (pancreatitis)
- Fungal infections, such as yeast infection or fungal infection of the nails
- Lung problems (such as edema)
- Fluid accumulation around the lungs (pleural effusion)
- Narrowed airway in the lungs, causing difficulty breathing
- Inflamed lining of the lungs, causing sharp chest pains that feel worse with breathing (pleurisy)
- Tuberculosis
- Kidney infections
- Low platelet count, too many white blood cells
- Infections of the vagina
- Blood test result showing ‘antibodies’ against your own body
- Changes in cholesterol and fat levels in the blood

Rare side effects: may appear in up to 1 out of 1,000 users

- Lymphoma (a type of blood cancer)
- Supply of oxygen from the blood to the body is insufficient, blood circulation problems, such as narrowing of blood vessels
- Inflammation of the lining of the brain (meningitis)
- Infection due to a weakened immune system

- Hepatitis B infection, if you have had such an infection in the past
- Inflamed liver caused by a problem with the immune system (autoimmune hepatitis)
- Liver problem that causes yellowing of the skin or the eyes (jaundice)

- Abnormal tissue swelling or growth
- Severe allergic reaction that may cause loss of consciousness and could be life-threatening (anaphylactic shock)

- Swelling of small blood vessels (vasculitis)
- Immune system problems that could affect the lungs, skin and lymph nodes (such as sarcoidosis)
- Accumulation of the immune system cells resulting from an inflammatory response (granulomatous lesions)
- Lack of interest or emotion
- Serious skin problems, such as toxic epidermal necrolysis, Stevens-Johnson syndrome and acute generalised exanthematous pustulosis

- Other skin problems, such as erythema multiforme, blisters and peeling skin, or boils (furunculosis)
- Serious nervous system disorders, such as transverse myelitis, multiple sclerosis-like disease, optic neuritis and Guillain-Barré syndrome
- Inflammation in the eye that may cause changes in the vision, including blindness

- Fluid in the lining of the heart (pericardial effusion)
- Serious lung problems (such as interstitial lung disease)
- Melanoma (a type of skin cancer)
- Cervical cancer
- Low blood count, including a severely decreased number of white blood cells
- Small red or purple spots caused by bleeding under the skin

- Abnormal values of a blood protein called “complement factor” which is part of the immune system
- Lichenoid reactions (itchy reddish-purple skin rash and/or threadlike white-grey lines on mucous membranes)

Side effects with unknown frequency: The frequency cannot be determined from the available information

- Cancer
- A rare blood cancer appearing mostly in teenage male adolescents or young men (hepatosplenic T-cell lymphoma)
- Liver failure
- Merkel cell carcinoma (a type of skin cancer)
- Kaposi’s sarcoma, a rare cancer related to infection with human herpes virus 8. Kaposi’s sarcoma most commonly appears as purple lesions on the skin
- Worsening of a condition called dermatomyositis (seen as a skin rash accompanying muscles weakness)
- Heart attack
- Stroke
- Temporary loss of sight during or within 2 hours of the infusion
- Infection due to a ‘live’ vaccine because of a weakened immune system

If a side effect occurs, if one side effect worsens or if you suffer from a side effect not mentioned in this leaflet, consult the physician.

Reporting of side effects:

Side effects can be reported to the Ministry of Health by clicking on the link “Report Side Effects of Drug Treatment” found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects or by entering on the following link: <https://sideeffects.health.gov.il>

Additionally, side effects can be reported to Padagis via the following address: Padagis.co.il

5.HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine and any other medicine must be stored in a safe place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the physician.

- Do not use the medicine after the expiry date (exp. date) that appears on the label and on the package. The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C to 8°C). Do not freeze! Keep the medicine in the original package to protect from light.

- This medicine can also be stored in the original package outside a refrigerator up to a maximum temperature of 25°C for a single period of up to 28 days. In this situation, the medicine should not be returned to refrigerated storage again. Dispose of medicine if it was not used during the 28 days period.

Write the date the medicine was removed from the refrigerator on the carton including day/month/year. Dispose of this medicine if not used by the end of the 28 days period or by the expiry date printed on the package, whichever is earlier.

- Medicines should not be disposed of via wastewater or household waste. Ask the pharmacist how to dispose of medicines no longer in use. This will help protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:

Sorbitol, sodium acetate trihydrate, polysorbate 80, acetic acid, water for injection.

What does the medicine look like and what are the contents of the package:

Remsima 120 mg/ml S.C. is a clear to opalescent, colorless to pale brown solution which is supplied as a single use pre-filled pen.

Each package contains: one pre-filled pen with 2 alcohol pads or 2 pre-filled pens with 2 alcohol pads or 4 pre-filled pens with 4 alcohol pads.

Not all package sizes may be marketed.

Registration holder: Padagis Israel Agencies Ltd., 1 Rakefet St., Shoham.

Manufacturer: Celltrion Ltd., Incheon, South Korea. Revised in March 2023 according to MOH guidelines.

Registration number of the medicine at the National Drug Registry of the Ministry of Health: 16727.36349

Instructions for use

Read these instructions carefully before using Remsima 120 mg/ml S.C. pen. Consult your physician if you have questions regarding the use of Remsima 120 mg/ml S.C. pen.

Important information

- Use the pen **ONLY** if your physician or nurse has trained you on the right way to receive the injection.
- Ask your physician how often you will need to inject.
- Change the injection site each time you inject. Each new injection site should be at least 3 cm away from the previous injection site.
- **Do not** use the pen if it has been dropped or if it is visibly damaged. A damaged pen may not function properly.
- **Do not** reuse the pen.
- **Do not** shake the pen at any time.

About Remsima 120 mg/ml S.C. pen

Parts of the pen (see Figure A)

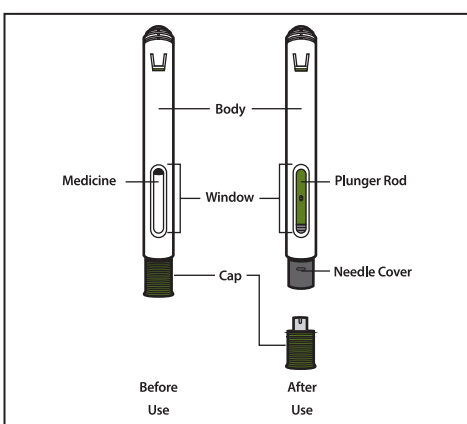


Figure A

- **Do not** remove the cap until you are ready to inject. Once the cap is removed, **do not** recap the pen.

Preparation for injection

1. Gather the required supplies for the injection.

- a. Prepare a clean and flat surface, such as a table or countertop, in a well-lit area.
- b. Remove the pen from the carton box stored in the refrigerator.
- c. Ensure that you have the following supplies:
 - Pen
 - Alcohol pad
 - Cotton ball or gauze*
 - Adhesive bandage*
 - Sharps disposal container*** Items not included in the carton box.*

2. Inspect the pen.

Do not use the pen if:

- The pen is cracked or damaged.
- The expiration date has passed.

3. Inspect the medicine (see Figure B).

The liquid should be clear and colorless to pale brown.

Do not use the pen if the liquid is cloudy, discolored or contains particles in it.

Note: You may see air bubbles in the liquid. This is normal.

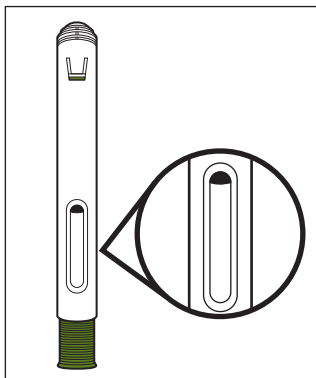


Figure B

4. Wait 30 minutes.

- a. Leave the pen at room temperature for 30 minutes to allow the solution to naturally warm up. **Do not** warm the pen using heat sources such as hot water or a microwave.

5. Choose the injection site (see Figure C).

- a. Select an injection site. You may inject into:
 - The front of the thighs.
 - The abdomen except for 5 cm around the belly button.
 - The outer area of the upper arms (to be performed by a caregiver or a healthcare professional **only**).

Do not inject into skin that is within 5 cm of your belly button, or is tender, damaged, bruised or scarred.

Note: Change the injection site each time you inject. Each new injection site should be at least 3 cm away from the previous injection site.

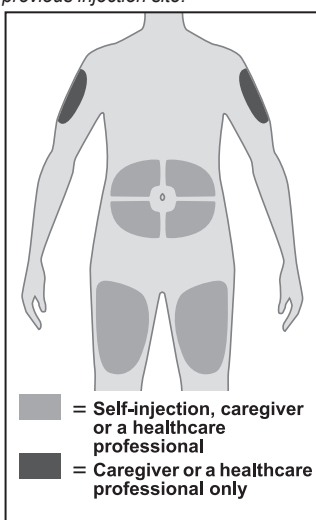


Figure C

6. Wash your hands.

- a. Wash your hands with soap and water and dry them thoroughly.

7. Clean the injection site.

- a. Clean the injection site with an alcohol pad.
- b. Let the skin dry before injecting.

Do not blow on the injection site or touch the injection site again before the injection.

Giving the injection

8. Remove the cap (see Figure D).

- a. Pull the olive green cap straight off and set it aside. **Do not** touch the needle cover. Touching the needle cover may result in a needle stick injury. *Note: It is normal to see a drop of liquid at the end of the needle.*

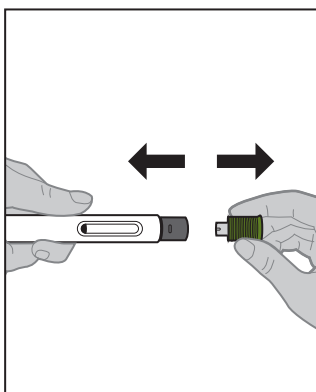


Figure D

9. Place the pen on the injection site (see Figure E).

- a. Hold the pen so that you can see the window.
- b. Without pinching or stretching the skin, place the pen over the injection site at a 90-degree angle.

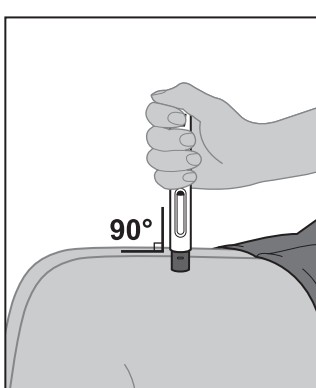


Figure E

10. Start the injection (see Figure F).

- a. Press the pen **firmly** against the skin. *Note: When the injection starts you will hear the 1st loud "click" and the olive green plunger rod will begin to fill the window.*
- b. Keep holding the pen **firmly** against the skin and listen for the 2nd loud "click".

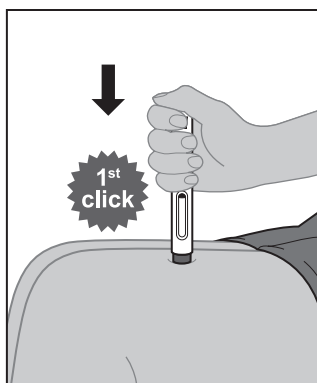


Figure F

11. Finish the injection (see Figure G).

- a. After you hear the 2nd loud "click", **continue to hold the pen firmly against the skin and count slowly to at least 5** to ensure you inject the full dose.

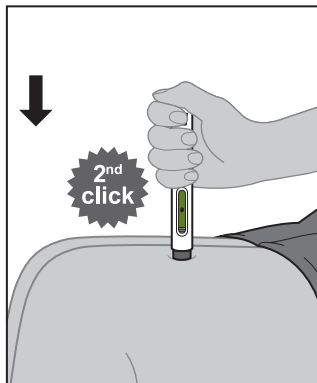


Figure G

12. Remove the pen from the injection site.

- a. Look at the pen and confirm that the olive green plunger rod is filling the window completely.
- b. Lift the pen from the injection site (see Figure H).
- c. Gently press a cotton ball or gauze over the injection site and apply an adhesive bandage, if necessary.

Do not rub the injection site.

Note: After removing the pen from the injection site, the needle will be automatically covered (see Figure I).

Note: If the olive green plunger rod does not fill the window completely, you did not receive your full dose. Do not reuse the pen in this case. Call your physician immediately.

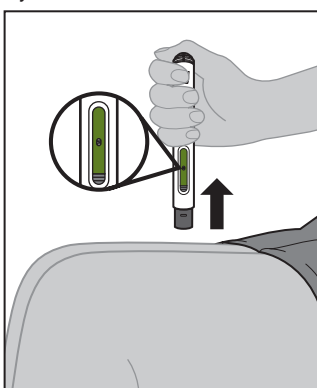


Figure H

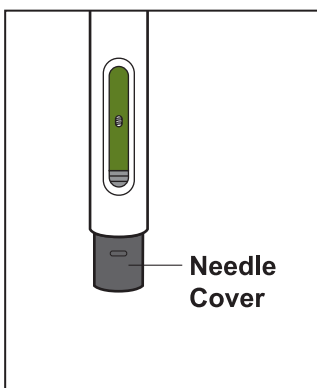


Figure I

After the injection

13. Dispose of the pen (see Figure J).

- Dispose of the used pre-filled pen in a special container as your physician, nurse or pharmacist instructed you.
- **Do not** recycle or dispose of the pre-filled pen via household waste.
- **Always** keep the pre-filled pen and the special container out of the reach and sight of children.

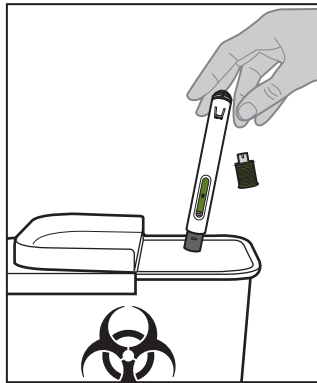


Figure J