Patient Package Insert in Accordance with the Pharmacists' Regulations (Preparations) - 1986
This medicine can be sold with a physician's prescription only

Remsima 120 mg/ml S.C.

Solution for subcutaneous injection in a pre-filled pen

The active ingredient and its quantity:
Each 1 ml of a single dose in a pre-filled pen contains 120 mg infliximab.
Inactive ingredients and allergens in the medicine: see section 6.

Read this entire leaflet carefully before using this medicine. This leaflet contains concise information about the medicine. If you have any further questions, ask the physician or pharmacist.
This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them even if you think that their illness is the same as yours.

Remsima 120 mg/ml S.C. is a biosimilar product. For further information on biosimilar products, please refer to the website of the Ministry of Health, Procedure 127 - Registration conditions and terms of use of biosimilar products.
http://www.health.gov.il/hozer/dr_127.pdf

In addition to the leaflet, a Patient Safety Information Card is available for Remsima 120 mg/ml S.C. This card contains important safety information which you must know and adhere to prior to beginning and during the treatment with Remsima 120 mg/ml S.C. Read the Patient Safety Information Card and the Patient leaflet before using the product. Keep the card for further reference if required.

1. What is the medicine intended for?

Rheumatoid arthritis:
Remsima 120 mg/ml S.C., in combination with methotrexate, is indicated for the reduction of signs and symptoms as well as the improvement in the physical function in:
- adult patients with active disease when the response to disease-modifying antirheumatic drugs (DMARDs), including methotrexate, has been inadequate.
- adult patients with a severe, active and progressive disease not previously treated with methotrexate or other DMARDs.

In these patient populations a reduction in the rate of the progression of joint damage, as measured by X-ray, has been demonstrated.

Therapeutic group: Immunosuppressants, TNFα inhibitors.
Remsima 120 mg/ml S.C. contains an active ingredient called infliximab, which is a monoclonal antibody- a type of protein which binds to a defined target in the body called TNF alpha (tumor necrosis factor alpha).
Remsima 120 mg/ml S.C. belongs to a group of medicines called 'TNF blockers' and works by selective binding to TNF alpha and blocking its action.
TNF alpha is involved in inflammatory processes in the body so blocking it can reduce the inflammation in your body.

2. Before using the medicine

Do not use the medicine if:
- You are hypersensitive (allergic) to infliximab or to any of the other ingredients this medicine contains (the ingredients are listed in section 6).
- You are allergic to proteins originating from mice.
- You have tuberculosis (TB) or another serious infection such as sepsis (serious bacterial infection of the blood), abscesses, and opportunistic infections (see section "Special warnings").
- You have heart failure that is moderate or severe.

Do not use Remsima 120 mg/ml S.C. if you suffer from one of the conditions listed above. If you are not sure, contact the physician before receiving Remsima 120 mg/ml S.C.

Special warnings regarding the use of the medicine
Before treatment with Remsima 120 mg/ml S.C., tell the physician if:
You have been treated in the past with any medicine containing infliximab
- Tell your physician if you have had treatment with medicines containing infliximab in the past and are now about to start treatment with Remsima 120 mg/ml S.C. again.
- If you stopped treatment with infliximab for more than 16 weeks, there is a higher risk of allergic reactions occurring when you start the treatment again.

Local reactions at the injection site
- Some of the patients receiving infliximab via subcutaneous injection have experienced local injection site reactions. Signs of a local injection site reaction can include redness, pain, itching, swelling, hardness, bruising, bleeding, cold sensation, tingling sensation, irritation, rash, ulcer, hives, blisters and scab on the skin of the injection site.
- Most of these reactions are mild to moderate and mostly resolve on their own within a day.

Infections
- Before starting treatment with Remsima 120 mg/ml S.C., tell your physician if you suffer from any infection, even if it is a very minor one.
- Before starting treatment with Remsima 120 mg/ml S.C. tell your physician if you have ever lived in or travelled to an area where the following infections are common: histoplasmosis, coccidioidomycosis or blastomycosis. These infections are caused by specific types of fungi that can damage the lungs or other parts of the body.
- The likelihood of you suffering from infections is higher during the course of treatment with Remsima 120 mg/ml S.C. If you are 65 years of age or older, you have a greater risk.
- The following infections, which may be serious, include: tuberculosis, infections caused by viruses, fungi, bacteria or other organisms in the environment and sepsis, that may be life-threatening.

Tell your physician straight away if you are suffering from signs of infection during the treatment with Remsima 120 mg/ml S.C. The signs include: fever, cough, flu-like signs, generally feeling unwell, hot or red skin, wounds or dental problems. Your physician may recommend temporarily stopping the treatment with Remsima 120 mg/ml S.C.

Tuberculosis (TB)
- It is very important that you tell your physician if you have ever had TB, or if you have been in close contact with someone who has or has had TB in the past.
- Your physician will test you to see if you have TB. Cases of TB have been reported in patients treated with infliximab, even in patients who have already been treated with medicines for TB. Your physician will record the test results on your "Patient Safety Information Card".
- If your physician feels that you are at risk for TB, you may be treated with medicines for tuberculosis before you start using Remsima 120 mg/ml S.C.

Tell your physician straight away if signs of TB occur during treatment with Remsima 120 mg/ml S.C. These signs include persistent cough, weight loss, feeling tired, fever, night sweats.

Hepatitis B virus (HBV)
- Before you receive treatment with Remsima 120 mg/ml S.C., tell your physician if you are a carrier of hepatitis B or have ever had hepatitis B virus.
- Tell your physician if you think you might be at risk of contracting hepatitis B virus.
- Your physician should test you for hepatitis B virus.
- The treatment with TNF blockers, such as Remsima 120 mg/ml S.C., may result in reactivation of hepatitis B virus in patients who carry this virus, and might be life-threatening in some cases.
- If you experience reactivation of hepatitis B, your physician may need to stop your treatment with Remsima 120 mg/ml S.C. and may give you medicines, such as an effective antiviral therapy with supportive treatment.

Heart problems
- Tell your physician if you have any heart problems, such as mild heart failure.
- Your physician will closely monitor your heart.

Tell your physician straight away if you experience new symptoms or worsening of existing symptoms of heart failure during treatment with Remsima 120 mg/ml S.C. The symptoms include shortness of breath or swelling of your feet.

Cancer and lymphoma
- Tell your physician before you are given Remsima 120 mg/ml S.C., if you have or have ever had lymphoma (a type of blood cancer) or any other type of cancer.
- Patients with severe rheumatoid arthritis who have had it for a long time, may be at higher risk of developing lymphoma.
- Patients taking Remsima 120 mg/ml S.C., may have a higher risk of developing lymphoma or another type of cancer.
- Some patients who have received TNF-blockers, including infliximab, have developed a rare type of cancer called hepatosplenic T-cell lymphoma. Of these patients, most were teenage boys or young men and most had Crohn's disease or ulcerative colitis. This type of cancer has usually resulted in death. Almost all patients had also received medicines containing azathioprine or mercaptopurine, in addition to TNF blockers.
- Some patients treated with infliximab have developed certain kinds of skin cancer. If you notice changes in your skin or growths on the skin during the treatment or after its completion, tell your physician.
- Some women, treated with infliximab for rheumatoid arthritis, have developed cervical cancer. For women taking Remsima 120 mg/ml S.C., including women over the age of 60, the physician may recommend regular screening for cervical cancer.

Lung disease or heavy smoking
- Tell your physician before you are given Remsima 120 mg/ml S.C., if you have a lung disease called chronic obstructive pulmonary disease (COPD) or if you are a heavy smoker.
- Patients with COPD and patients who are heavy smokers may be at a higher risk of developing cancer during treatment with Remsima 120 mg/ml S.C.

Nervous system diseases
- Tell your physician before you are given Remsima 120 mg/ml S.C., if you have or have had in the past problems that affects your nervous system. The problems include: Multiple sclerosis, Guillain-Barré syndrome, if you have fits or have been diagnosed with 'optic neuritis'.

Tell your physician straight away if you get symptoms of a nerve disease during the treatment with Remsima 120 mg/ml S.C. The signs include: changes in your vision, weakness in your arms or legs, numbness or tingling in any part of your body.

Abnormal skin openings (fistulae)
- Tell your physician if you have any abnormal skin openings (fistulae) before you are given Remsima 120 mg/ml S.C.

Vaccinations
- Tell your physician if you have recently had or are due to have a vaccine.
- You should receive recommended vaccinations before starting the treatment with Remsima 120 mg/ml S.C. You may receive some vaccines during treatment with Remsima 120 mg/ml S.C., but you should not receive 'live' vaccines (vaccine that contains a living but weakened infectious agent) during treatment with Remsima 120 mg/ml S.C., because it may cause infections.
- If you received Remsima 120 mg/ml S.C. during pregnancy, your baby may also be at a higher risk for getting an infection as a result of live vaccine up to 6 months after birth. It is important that you tell your baby's physicians and other healthcare professionals that you have used Remsima 120 mg/ml S.C. during pregnancy so they can decide when your baby should receive any vaccine, including 'live' vaccines such as BCG vaccine (used to prevent tuberculosis). For more information see section "Pregnancy, breastfeeding and fertility".

Therapeutic infectious agents
- Tell your physician if you have recently received or if you are scheduled to receive treatment with a therapeutic infectious agent (such as BCG vaccine used for the treatment of cancer).

Operations or dental procedures
- Tell your physician if you are going to have any operations or dental procedures.
- Tell your surgeon or dentist that you are having treatment with Remsima 120 mg/ml S.C., and show them your "Patient Safety Information Card".

Liver problems
- Some patients receiving infliximab have developed serious liver problems.
- Tell your physician straight away if you get symptoms of liver problems during treatment with Remsima 120 mg/ml S.C. The signs include yellowing of the skin and eyes, dark brown colored urine, pain or swelling in the upper right side of the stomach area, joint pain, skin rash or fever.

Low blood counts
- In some patients receiving infliximab, the body may not make enough of the blood cells that help fight infections or help stop bleeding.
- Tell your physician straight away if you get symptoms of low blood counts during the treatment with Remsima 120 mg/ml S.C. The signs include persistent fever, bleeding or bruising more easily, small red or purple spots caused by bleeding under the skin, or looking pale.

Immune system disorder
- Some patients receiving infliximab have developed symptoms of an immune system disorder called lupus.
- Tell your physician straight away if you develop symptoms of lupus during treatment with Remsima 120 mg/ml S.C. The signs include joint pain or a rash on the cheeks or arms that is sensitive to the sun.

Children and adolescents
Remsima 120 mg/ml S.C. is not intended for use in children or adolescents under the age of 18 since there is not enough data to support that this medicine is safe and effective in this age group.

Drug interactions
If you are taking, or have recently taken, other medicines including non-prescription medicines and nutritional supplements, tell the physician or pharmacist. Especially inform the physician or the pharmacist if you are taking or have previously taken:
- Medicines to treat inflammatory diseases. These medicines may cause side effects. Your physician will advise you on which other medicines you should continue taking while you are being treated with Remsima 120 mg/ml S.C.
- Medicines to treat Crohn's disease, ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, or medicines obtained without a prescription, such as vitamins and herbal remedies.

In particular, tell your physician if you are using any of the following medicines:
- Medicines that affect your immune system.
- Kineret (which contains anakinra). Remsima 120 mg/ml S.C. and Kineret should not be used at the same time.
- Orencia (which contains abatacept). Remsima 120 mg/ml S.C. and Orencia should not be used at the same time.

During the treatment with Remsima 120 mg/ml S.C. you should not receive 'live' vaccines. If you were using Remsima 120 mg/ml S.C. during the pregnancy, inform your baby's physician and other healthcare professionals who are treating your baby that you have been using Remsima 120 mg/ml S.C., before the baby is given any vaccines.
If you are not sure if any of the above applies to you, talk to your physician or the pharmacist before using Remsima 120 mg/ml S.C.

Pregnancy, breastfeeding and fertility
- You should consult your physician before using this medicine if you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby. The information for use in pregnancy is limited. Remsima 120 mg/ml S.C. should only be used during the pregnancy if your physician thinks it is necessary for you.
- You should avoid getting pregnant while using Remsima 120 mg/ml S.C. and for 6 months after stopping treatment. Consult your physician regarding the use of contraception during this time.
- It is unknown whether infliximab is excreted in human milk or absorbed systemically after ingestion. Because human immunoglobulins are excreted in milk, do not breastfeed when you are being treated with Remsima 120 mg/ml S.C. or for 6 months after your last treatment with Remsima 120 mg/ml S.C.
- If you received Remsima 120 mg/ml S.C. during your pregnancy, your baby may have a higher risk for getting an infection.
- It is important that you tell your baby's physicians and other healthcare professionals about your Remsima 120 mg/ml S.C. use before your baby is given any vaccine. If you received Remsima 120 mg/ml S.C. during the pregnancy, giving BCG vaccine (used to prevent tuberculosis) to your baby within 6 months after birth may cause an infection with serious complications, including death. 'Live' vaccines such as BCG should not be given to your baby within 6 months after the birth. For more information see section "vaccinations".
- In infants born to women treated with infliximab during the pregnancy, a severe decrease in the numbers of white blood cells have been reported. If your baby has continual infections and fevers, contact your baby's pediatrician immediately.
- There are insufficient preclinical data to draw conclusions on the effects of infliximab on fertility and general reproductive function.

Driving and using machines
Remsima has a minor influence on the ability to drive and use machines. Side effect of dizziness may occur while using Remsima 120 mg/ml S.C. If you feel tired, dizzy, or unwell after receiving treatment with Remsima 120 mg/ml S.C., do not drive or use any tools or machines.

Important information about some of the ingredients of this medicine
Remsima 120 mg/ml S.C. contains sodium and sorbitol
This medicine contains less than 1 millimole (23 mg) of sodium per dose, i.e. it is essentially "sodium free" and contains 45 mg sorbitol in each 120 mg dose.

3. How to use the medicine?

Always use Remsima 120 mg/ml S.C. according to the physician's instructions. Check with the physician or pharmacist if you are not sure about the dosage and the treatment regimen with this medicine. The dosage and the treatment regimen will be determined by the physician only.

Rheumatoid arthritis
Your physician will start the treatment with 2 Remsima 100 mg I.V. intravenous infusion doses of 3 mg for every kg of body weight (given into your vein, usually in your arm, for 2 hours).
They are administered 2 weeks apart via intravenous infusion. After 4 weeks from the last intravenous infusion, you will be given the 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 2 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 2 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 2 weeks.
If you are not sure when to inject Remsima 120 mg/ml S.C., contact your physician.

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 a 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 eyes 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 people
- 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 people
- 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 people
- 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 stye
- 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

Rare side effects: may appear in up to 1 out of 1,000 people
- 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 appears, if one side effect gets worse or if you suffer from a side effect which is 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 "Reporting Side Effects from Drug Treatment" that can be found on the home page of the Ministry of Health website (www.health.gov.il) directing to the online form of adverse events reporting or by clicking on the following link: https://sideeffects.health.gov.il
Additionally, side effects can be reported to Perrigo via the following address: www.perrigo-pharma.co.il

5. How to store the medicine?
- Avoid poisoning! This medicine and any other medicine must be stored in a closed 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 14 days.
  In this situation, the medicine should not be returned to refrigerated storage again. Dispose of medicine if it was not used during the 14 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 until the end of the 14 days period or until the expiry date printed on the carton, 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. Additional 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 is 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: 1 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: Perrigo Israel Agencies Ltd., 1 Rakefet St., Shoham.
Manufacturer: Celltrion Ltd., Incheon, South Korea.
Approved in May 2021.
Registration number of the medicine at the National Drug Registry of the Ministry of Health: 16727.36349

Remsima 120 Pen PIL PB0521-14

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*)

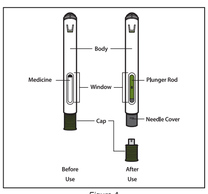

Figure A

- **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*).
Do not use the pen if the liquid is different from a clear colorless or pale brown or contains particles in it.
Note: You may see air bubbles in the liquid. This is normal.

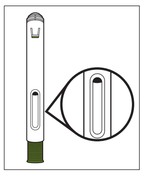
Figure B

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.

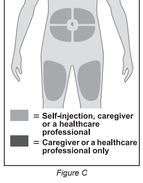

Figure C

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.

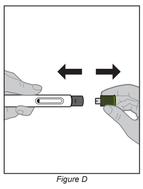
Figure D

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.

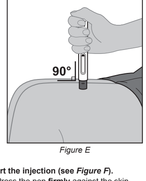

Figure E

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.

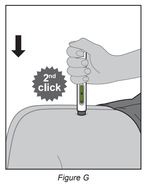

Figure G

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.

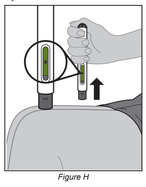
Figure H

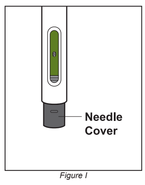

Figure I

After the injection
13. Dispose of the pen (see Figure J).
- Dispose of the used pre-filled pen in a special container as your doctor, 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 sight and reach of children.

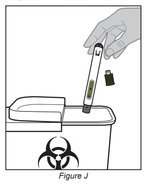
Figure J