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

This medicine is dispensed with a physician's prescription only

Remsima 100 mg I.V. Powder for concentrate for solution for

Each Remsima 100 mg I.V. vial contains 100 mg infliximab. After preparing the solution, each ml contains 10 mg infliximab. Inactive ingredients and allergens: see section 6 "Additional

Read the entire leaflet carefully before using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, refer to the physician or the pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that $% \left(x\right) =\left(x\right) +\left(x\right) =\left(x\right) +\left(x\right) +\left(x\right) =\left(x\right) +\left(x\right$ their illness is similar.

Remsima 100 mg I.V. is a biosimilar product. In addition to the leaflet, a Patient Safety Information Card is available for Remsima 100 mg I.V. This card contains important safety information which you must know and adhere to prior to beginning and during the treatment with Remsima 100 mg I.V. Read the Patient Safety Information Card and the Patient leaflet before using the product. Keep the card for further reference if required.

For adults:

For your attention, the Ministry of Health has approved a one time substitution between an innovative medicine and a biosimilar medicine and vice versa

medicine and vice versa.

The physician will provide you with an explanation regarding the medicine and the significance of the substitution. Any substitution with a biological medicine must be performed by your attending physician. The commercial name of the medicine which appears the recognition should be the commercial name. on the prescription should be the same as the commercial name which appears on the package of the medicine which was dispensed to you at the pharmacy. If in doubt, contact the pharmacist or your attending physician.

For children:

This product is not intended for use in children.

1. WHAT IS THE MEDICINE INTENDED FOR? Remsima 100 mg I.V. is used for the treatment of adults suffering

- from the following inflammatory diseases:
- Rheumatoid arthritis
- Ankylosing spondylitis (Bechterew's disease)
- Crohn's disease

Therapeutic group: TNF α blockers Remsima 100 mg I.V. contains the active substance called

Infliximab is monoclonal antibody - a type of protein that attaches to a specific target in the body, to a protein called TNF (tumour necrosis factor) alpha. Remsima 100 mg I.V. works by selectively attaching to TNF alpha

protein and blocking its action.

TNF alpha is involved in inflammatory processes of the body so

blocking it can reduce the inflammation in your body.

2. BEFORE USING THE MEDICINE Do not use this medicine if: • you are sensitive (allergic) to infliximab or to any of the other

- ingredients of this medicine (the ingredients are listed in
- you are allergic to proteins originating from mice.
 you have tuberculosis (TB) or another serious infection such as
- pneumonia or sepsis (serious bacterial infection of the blood). you suffer from moderate to severe heart failure.

Do not use Remsima 100 mg I.V. if you suffer from any of the conditions listed above. If you are not sure, talk to the physician before taking Remsima 100 mg I.V.

Special warnings regarding the use of this medicine Before treatment with the medicine, tell your physician if: You have been treated in the past with any medicine containing

Tell your physician if you have had treatment with medicines containing infliximab in the past and are now starting Remsima 100 mg I.V. treatment again.

• If you stopped treatment with infliximab for more than 16 weeks there is a higher risk of allergic reactions occurring when you start

- Infections:
 Before starting treatment with Remsima 100 mg l.V., tell the physician if you have any infection, even if it is a minor infection.

 Before starting treatment with Remsima 100 mg I.V., tell the physician
- if you ever have lived or travelled in 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 organs of the body.

 • The likelihood that you will suffer from infections is higher during the course of treatment with Remsima 100 mg I.V. If you are
- 65 years of age or older, you have a higher 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 have signs of infection during treatment with Remsima 100 mg I.V. The signs include: fever, cough, flu-like signs, generally unwell feeling, hot or red skin, wounds or dental problems. The physician may recommend temporary discontinuation of Remsima 100 mg I.V. treatment.

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
- The 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 anti-TB medications. The physician will record the results of the test in your Information Card".
- If your physician thinks that you are at risk for TB, you may be treated with anti-TB medicines before you start taking Remsima 100 mg I.V.

Tell your physician straight away if signs of TB occur during treatment with Remsima 100 mg I.V. These signs include persistent cough, weight loss, fatigue, fever, night sweats.

- Tell your doctor before you are given Remsima 100 mg I.V. if you are a carrier of hepatitis B or have ever had it.
- Tell your doctor if you think you might be at risk of contracting HBV. Your physician should test you for HBV.
- Treatment with TNF blockers, such as Remsima 100 mg I.V., may result in reactivation of hepatitis B virus in patients who carry this virus, which can be life-threatening in some cases If you experience reactivation of hepatitis B, your doctor may need
- to stop your treatment with Remsima 100 mg I.V. and may give you medicines such as effective antiviral therapy with supportive

Heart problems

• Tell the physician if you have any heart problems, such as mild heart failure. The physician will closely monitor your heart.

Tell the physician straight away if you experience new heart failure symptoms or if preexisting heart failure symptoms worsen during treatment with Remsima 100 mg I.V. Symptoms include shortness of breath or swelling of the legs

Cancer and lymphoma • Tell your physician before you are given Remsima 100 mg I.V., 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 the
- disease for a long time, may be at higher risk of developing · Adults taking Remsima 100 mg I.V. may have 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 either Crohn's disease or ulcerative colitis. This type of cancer usually resulted in death. Almost all patients had also received medicines containing azathioprine or mercaptopurine in addition to TNF-blockers.
- Certain patients treated with infliximab developed certain kinds of skin cancer. If you notice changes in your skin or growths on the
- skin during treatment or after its completion, tell your physician. Some women being treated for rheumatoid arthritis with infliximab have developed cervical cancer. For women taking Remsima 100 mg I.V., including women over the age of 60, the doctor may recommend to be regularly screened for cervical

Lung disease or heavy smoking

- Tell your physician before you are given Remsima 100 mg I.V., 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 the course of Remsima 100 mg I.V. treatment.

Nervous system diseases

• Tell your physician before you are given Remsima 100 mg I.V., if you have or have ever had problems that affect your nervous system. These problems include: multiple sclerosis. Guillain-Barré syndrome, if you have fits or if you have been diagnosed with optic

Tell your physician straight away if you get symptoms of a nerve disease during treatment with Remsima 100 mg I.V. Signs include: changes in vision, weakness in arms or legs, numbness or tingling in any part of the body.

Abnormal skin openings (fistulae)

• Tell your physician if you have any abnormal skin openings (fistulae), before you are given Remsima 100 mg I.V.

Vaccinations

- Tell your physician if you recently received or are due to receive a vaccination.
- You should receive recommended vaccinations before starting Remsima 100 mg I.V. treatment. You may receive some vaccines during treatment with Remsima 100 mg I.V. but you should not receive 'live' vaccines (vaccines that contain a living but weakened infectious agent) while using Remsima 100 mg I.V. because they may cause infections.
- If you received Remsima 100 mg I.V. while pregnant, your baby may also be at higher risk of getting an infection as a result of a live vaccination up to approximately six months after birth. It is important that you tell your baby's physicians and other healthcare professionals that you used Remsima 100 mg I.V. during pregnancy, so they can decide when to give your baby any vaccination, including 'live' vaccines such as BCG (used to prevent tuberculosis). For more information, see "Pregnancy, breastfeeding and fertility" section.

Therapeutic infectious agents

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

Operations or dental procedures Tell your physician if you are about to undergo any operation or

dental procedure.

Tell the surgeon or dentist that you are having treatment with Remsima 100 mg I.V., and show them your "Patient Safety Information Card".

Liver problems • Some patients receiving infliximab have developed serious liver problems.

• Tell your doctor straight away if you get symptoms of liver problems

the upper right side of the stomach area, joint pain, skin rashes

Low blood count

during treatment with Remsima 100 mg I.V. Signs include yellowing of skin and eyes, dark-brown coloured urine, pain or swelling on

 In some patients receiving infliximab, the body may not make enough blood cells that help fight infections or help stop bleeding.
 Tell your doctor immediately if you have symptoms of low blood counts during treatment with Remsima 100 mg I.V. Signs include persistent fever that does not go away, 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 doctor straight away if you develop symptoms of Lupus during treatment with Remsima 100 mg I.V. Signs include joint pain or a rash on the cheeks or arms that is sensitive to the sun.

If you are not sure if any of the above apply to you, talk to your physician before receiving Remsima 100 mg I.V. treatment.

- Tell your physician if you are a heavy smoker, before you receive Remsima 100 mg I.V.
- · Patients who are heavy smokers may be at a higher risk of developing cancer as a result of Remsima 100 mg I.V. treatment.

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, inform the physician or pharmacist. In particular, inform the physician or the pharmacist if you are taking or have taken in the past:

• Medicines to treat inflammatory diseases. These medicines may

- cause side effects. Your physician will advise you which other medicines you should continue using while receiving Remsima 100 mg I.V. treatment.

 Medicines to treat Crohn's disease, ulcerative colitis, rheumatoid
- arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis or medicines given without a prescription, such as vitamins and herbal medicines In particular, tell the physician if you are using any of the following

- Medicines that affect your immune system. • Kineret (which contains anakinra). Do not use Remsima 100 mg I.V.
- and Kineret together. Orencia (which contains abatacept). Do not use Remsima 100 mg I.V.
- and Orencia together. During treatment with Remsima 100 mg I.V. you should not receive 'live' vaccines. If you were using Remsima 100 mg I.V.
- during pregnancy, tell your baby's doctor and other healthcare professionals caring for your baby that you used Remsima 100 mg I.V., before the baby receives any vaccination. If you are not sure if any of the above applies to you, talk to your

physician or pharmacist before using Remsima 100 mg I.V

Pregnancy, breastfeeding and fertility • If you are pregnant or breastfeeding, think you may be pregnant

- or are planning to become pregnant, consult your physician before taking the medicine. Remsima 100 mg I.V. should only be used during pregnancy if the physician feels it is necessary for you.
- Avoid getting pregnant during the course of treatment with Remsima 100 mg I.V. and for 6 months after stopping treatment. Consult your physician regarding use of contraception during this
- Do not breastfeed when you are being treated with Remsima 100 mg I.V. or for 6 months after stopping treatment. If you received Remsima 100 mg I.V. during pregnancy, your baby
- may be at a higher risk for getting an infection.
- It is important that you tell your baby's doctors and other healthcare professionals about your Remsima 100 mg I.V. use before your baby is given any vaccine. If you received Remsima 100 mg l.V. while pregnant, giving BCG vaccine (used to prevent tuberculosis) to your baby within 6 months after birth may result in infection with serious complications, including death. 'Live' vaccines such as BCG should not be given to your baby within 6 months after birth. For more information see "vaccination" section. Severely decreased numbers of white blood cells have been
- reported in infants born to women treated with infliximab during pregnancy. If your baby has continual infections and fevers, refer to your baby's doctor immediately.

Driving and using machines Remsima 100 mg I.V. is not likely to affect your ability to drive,

use tools or operate machines. If you feel tired, dizzy or unwell after receiving Remsima 100 mg I.V. treatment, do not drive or use any tools or machines. Important information about some of the medicine's

This medicine contains less than 23 mg sodium per dose, i.e. it is essentially 'sodium-free'.

However, before Remsima 100 mg I.V. is given to you, it is mixed with a solution that contains sodium. Talk to your doctor if you are on a low salt diet.

3. HOW IS REMSIMA 100 MG I.V. GIVEN? • Remsima 100 mg I.V. will be given to you by a physician or nurse, in a hospital or clinic.

- Your physician or nurse will prepare the solution for infusion. The Remsima 100 mg I.V. solution will be given to you as an infusion (drip) (over a 2 hour period) into one of your veins usually
- in the arm. After the third treatment, the physician may decide to give you the dose of the solution over a 1 hour period only. You will be under medical surveillance while receiving Remsima 100 mg I.V. and for 1 to 2 hours after as well.
- Your physician will determine the dosage (in mg) and how often
- you will receive Remsima 100 mg I.V., in accordance with your disease, your weight and your response to Remsima 100 mg I.V.

If you received too much Remsima 100 mg I.V. As this medicine is given by a nurse or physician, it is unlikely that you will be given an overdose of the medicine. There are no

dosage of Remsima 100 mg I.V.

If you forget or miss an appointment to receive Remsima 100 mg I.V.,

make another appointment as soon as possible. Adhere to the treatment as recommended by the physician.
Even if there is improvement in your health, do not stop treatment with this medicine without consulting the physician.

known side effects associated with administration of too high

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

4. SIDE EFFECTS As with any medicine, Remsima 100 mg I.V. use may cause side

effects in some users. Do not be alarmed by reading the list of side effects. You may not experience any of them.

Most side effects are mild to moderate. However, some patients may experience serious side effects and may require treatment. Side effects may also occur after stopping treatment with Remsima 100 mg I.V.

Refer to a physician straight away if you notice any of the

- 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, legs or ankles. Some of these reactions may be severe or life-threatening. An allergic reaction could happen within 2 hours of receiving the injection or later. More signs of allergic side effects that may happen up to 12 days after your injection include: pain in the muscle, fever, jaw or joint pain, sore throat or headache.
- 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 the chest, a fast or a slow heartbeat and swelling of
- Signs of infection (including TB) such as fever, tiredness, cough which may be persistent, shortness of breath, flu-like symptoms, weight loss, night sweats, diarrhea, wounds, collection of pus in the gut or around the anus (abscess), dental problems or burning sensation upon 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 colouring, or unusual vaginal bleeding.

 • Signs of lung problems such as coughing, breathing difficulties
- 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 severe headache), fits, tingling/numbness in any part of the body, or weakness in 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 and eyes, dark-brown colored urine, pain or swelling in the upper right side of the stomach, joint pain, skin rashes or fever.

 • Signs of an immune system disorder called Lupus such as
- joint pain or a rash on the cheeks or arms that is sensitive to the sun (Lupus) or cough, shortness of breath, fever or skin rash Signs of a low blood count such as persistent fever, bleeding or bruising more easily, small red or purple marks 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 of 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 the doctor straight away if you notice any of the above.

The following side effects have been observed with Remsima

100 mg I.V. Very common side effects: may occur in more than 1 in 10 people

Stomach pain, nausea

or tightness in the chest

- Viral infection, such as herpes or fluUpper respiratory tract infection, such as sinusitis
- Headache Side effects due to the infusion
- Common side effects: may occur in up to 1 in 10 people · Changes in liver function, increase in liver enzymes (shown in hlood tests)
- Lung or chest infection, such as bronchitis or pneumonia Difficult or painful breathing, chest pain
 Bleeding in the stomach or intestines, diarrhea, indigestion,
- heartburn, constipation
- Urticaria (hives), itchy rash or dry skin • Balance problems or feeling dizzy
- Fever, increased sweating Circulation problems such as low or high blood pressure Bruises, hot flushes or nosebleed, hot and red skin (flushing)
- Feeling tired or weak
- Bacterial infection such as sepsis, 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, sleeping problems
 Eye 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, causing swelling
- Numb or tingling sensation

Uncommon side effects: may occur in up to 1 in 100 people Shortage of blood supply, swelling of a vein

- Collection of blood outside the blood vessels (haematoma) or bruising • Skin problems such as blistering, warts, abnormal skin colouration 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 of forgetfulness, irritability, confusion, nervousness • Eye problems including blurred or reduced vision, puffy eyes or
- Convulsions, nerve problems A hole in the intestine or blockage of the intestine, stomach pain

New or worsening heart failure, slow heart rate

 Swelling of the pancreas (pancreatitis) Fungal infections such as candida, or fungal infection of the nails

Fainting

Tuberculosis

Kidney infections

(autoimmune Hepatitis)

- Lung problems (such as edema) Fluid around the lungs (pleural effusion)
- Narrowed airway in the lungs, causing difficulty breathing • Inflamed lining of the lung, causing sharp chest pains that feel worse with breathing (pleurisy)
- Low platelet count, too many white blood cells Infections of the vagina Blood test result showing 'antibodies' against your body

Rare side effects: may occur in up to 1 in 1,000 people Lymphoma (a type of blood cancer)

- Inadequate oxygen supply from the blood to the body, blood circulation problems such as narrowing of blood vessels Inflammation of the lining of the brain (meningitis)
- Infection due to weakening of the immune system • Hepatitis B infection, if you have had such an infection in the past • Inflammation of the liver due to a problem in the immune system
- Liver problem that causes yellowing of the skin or 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) Collections of immune cells resulting from an inflammatory response (granulomatous lesions)
- ack of interest or emotion Serious skin problems such as Lvell's disease (toxic epidermal necrolysis), Stevens-Johnson syndrome and pustules of type

peeling of skin, or boils (furunculosis)

Acute Generalised Exanthematous Pustulosis (AGEP) • Other skin problems such as erythema multiforme, blisters and

- If you forget or miss a Remsima 100 mg I.V. infusion

Cervical cancer

- Merkel cell carcinoma (a type of skin cancer)
- Worsening of a condition called dermatomyositis (seen as a skin
- Heart attack
- Temporary loss of sight during or within 2 hours of infusion
 Infection due to 'live' vaccines because of a weakened immune
- If a side effect occurs, if any of the side effects gets worse, or if you suffer from a side effect not mentioned in the leaflet, consult the physician.

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

Remsima 100 mg I.V. will be stored by the healthcare professionals at the hospital or in the clinic. The storage details, should you need them, are as follows:

• Avoid poisoning! This medicine and any other medicine should be

infants in order to avoid poisoning. Do not induce vomiting without an explicit instruction from the

pnysician.
Do not use this medicine after the expiry date (exp. date) which is stated on the label and package. The expiry date refers to the last day of that month. Even if stored as recommended, medicines may be kept for a limited period only. Please note the expiry date of the medicine! In case of doubt, consult the pharmacist who dispensed the medicine to you.

to use the solution as soon as possible (within 3 hours). However,

if the solution is prepared in a germ-free environment, it can be stored in a refrigerator at 2°C to 8°C for 24 hours. Do not use the solution if it is discolored or if there are particles in it. Do not discard the medicine to the wastewater or household waste.

6. ADDITIONAL INFORMATION

In addition to the active ingredient the medicine also contains: Sucrose, disodium hydrogen phosphate dihydrate, sodium

package: Remsima 100 mg I.V. is supplied in a glass vial containing a white powder for preparation of the concentrate for solution for infusion. Remsima 100 mg I.V. is marketed in a pack containing one vial.

Manufacturer: Celltrion Ltd., Incheon, South Korea.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 15460.34158

Remsima 100 mg I.V. PIL PB0521-05

Abnormal values of a blood protein called "Complement Factor"

Serious nervous system problems, such as transverse myelitis

Inflammation in the eye that may cause changes in the vision,

multiple sclerosis-like disease, optic neuritis and Guillain-Barré

- Low blood counts, including a severely decreased number of white Small red or purple spots caused by bleeding under the skin.

Fluid in the lining of the heart (pericardial effusion)

Melanoma (a type of skin cancer)

Serious lung problems (such as interstitial lung disease)

- which is part of the immune system
 Lichenoid reactions (itchy reddish-purple skin rash and/or
- Side effects of unknown frequency: frequency cannot be estimated from the available data

A rare blood cancer affecting mostly teenage boys or young males

(hepatosplenic T cell lymphoma)

threadlike white-grey lines on mucous membranes)

- 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.
- rash accompanied by muscle weakness)

Reporting of side effects:

following address: www.perrigo-pharma.co.il 5. HOW SHOULD THE MEDICINE BE STORED?

kept in a closed place out of the reach and sight of children and/or physician.

- Store in the original package.
 Store in a refrigerator (2°C to 8°C). • After preparing Remsima 100 mg l.V. for infusion, it is recommended
- Consult the pharmacist about how to dispose of the medicine. This will help protect the environment.

dihydrogen phosphate monohydrate, polysorbate 80. What the medicine looks like and the contents of the

Registration holder: Perrigo Israel Agencies Ltd., 1 Rakefet St.,

Revised in June 2021 according to MOH guidelines.