PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

Name of the medicine, its form and strength

Remicade®

100 mg powder for preparation of concentrate for solution for infusion

The active substance and its quantity: Each vial contains 100 mg of infliximab

Infliximab, 100 mg

Inactive and allergenic substances in the preparation: see section 2 "Important information about some of the ingredients of the medicine" and section 6 "Further Information".

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them, even if it seems to you that their ailment is similar.

In addition to the leaflet, for the preparation Remicade, there is a Patient Reminder Card. This card contains important safety information which you need to know before commencing treatment with Remicade and during treatment, and to act accordingly. Read the Patient Reminder Card and the patient leaflet before beginning to use the preparation. Keep the card for further reference if needed.

For adults:

Please note that the Ministry of Health has approved a once-only substitution between an original and a biosimilar medicine, and the reverse.

The doctor will provide you with an explanation of the medicine and the significance of the substitution. Any substitution of a biological medicine must be done by the attending doctor. The trade name of the medicine that appears in the prescription must be identical to the trade name that appears on the medicine package supplied to you at the pharmacy. In any case of doubt, refer to the pharmacist or the attending doctor.

For children:

Please note that it is important that every time you receive the medicine at the pharmacy, you ascertain that you are receiving the same medicine that was prescribed by the specialist doctor who treats you. If the medicine that you received appears different from that which you usually receive or if the instructions for use have changed, please refer immediately to the pharmacist to ensure that you have received the correct medicine. Any

substitution or dosage change of a medicine containing infliximab (the active substance in the medicine) must only be done by the patient's specialist doctor.
Please check that the trade name of the preparation that the specialist doctor wrote in the prescription is identical to the name of the medicine that you received from the pharmacist.

1. WHAT IS THE MEDICINE INTENDED FOR?

Crohn's disease in adults:
For the treatment of active, moderate to severe Crohn's disease in patients who did not respond to full and adequate therapy with corticosteroids and/or immunosuppressants.
For the treatment of fistulizing Crohn's disease in patients who did not respond to full and adequate conventional therapy.

Crohn's disease in children:
For the treatment of severe Crohn's disease in children aged 6-17 who did not respond to conventional therapy, including corticosteroids, immunomodulators and primary nutrition therapy, or who cannot tolerate or have a contraindication to these therapies.
Remicade has been studied only in combination with conventional immunosuppressive therapy.

Ankylosing spondylitis:
For the treatment of ankylosing spondylitis in patients who have severe axial symptoms, an elevated level of markers of inflammatory activity, and who did not respond adequately to conventional therapy.

Psoriatic arthritis:
For the treatment of active and progressive psoriatic arthritis in adults whose response to previous DMARDs therapy (**disease-modifying antirheumatic drugs**) was inadequate. Remicade is given in combination with methotrexate, or alone in patients who cannot tolerate methotrexate or who have a contraindication to methotrexate. Remicade improved the physical function in patients with psoriatic arthritis and reduced the rate of progression of the peripheral joint damage, measured by x-ray, in patients with the symmetrical polyarticular subtype of the disease.

Rheumatoid arthritis:
Remicade, in combination with methotrexate, is indicated for the reduction of signs and symptoms and to improve physical function in patients with active disease who did not respond adequately to DMARDs including methotrexate. For patients with progressive, active and severe disease who were not previously treated with methotrexate or other DMARDs, a reduction in the rate of progression of joint damage was demonstrated, measured by x-ray in these populations.

Psoriasis:
For the treatment of moderate to severe plaque psoriasis in adults for whom other systemic therapy, including ciclosporin, methotrexate or PUVA, has failed, or who are intolerant or have a contraindication to these therapies.

Ulcerative colitis:
For the treatment of active moderate to severe disease in patients with ulcerative colitis who did not respond adequately or who have intolerance or a contraindication to conventional therapy, including corticosteroids, 6-MP or AZA.

Ulcerative colitis in children:
For the treatment of active severe ulcerative colitis in children aged 6-17 years who did not respond adequately or who have intolerance or a contraindication to conventional therapy, including corticosteroids, 6-MP or AZA.

The active ingredient, infliximab, belongs to the group of immunosuppressants called TNF blockers, ATC code: L04AB02.

Therapeutic group: Remicade contains the active substance infliximab. Infliximab is a monoclonal antibody – a type of protein that attaches to a specific target in the body called TNF-α (tumour necrosis factor).

Remicade works by selectively attaching to TNF-α and blocking its action. TNF-α is involved in inflammatory processes of the body, so blocking it causes a reduction in the body's inflammation.

Rheumatoid arthritis
Rheumatoid arthritis is an inflammatory disease of the joints. If you suffer from active rheumatoid arthritis, you will first be treated with other medicines. If these medicines do not work well enough, you will be given Remicade, in combination with another medicine called methotrexate to:
- Reduce the signs and symptoms of the disease.
- Slow down the damage to joints.
- Improve physical function.

Psoriatic arthritis
Psoriatic arthritis is an inflammatory disease of the joints, usually accompanied by psoriasis. If you suffer from active psoriatic arthritis, you will first be treated with other medicines. If these medicines do not work well enough, you will be given Remicade to:
- Reduce the signs and symptoms of the disease.
- Slow down the damage to joints.
- Improve physical function.

Ankylosing spondylitis
Ankylosing spondylitis is an inflammatory disease of the spine. If you suffer from ankylosing spondylitis, you will first be treated with other medicines. If these medicines do not work well enough, you will be given Remicade to:
- Reduce the signs and symptoms of the disease.

- Improve physical function.

Psoriasis

Psoriasis is an inflammatory disease of the skin. If you suffer from moderate to severe psoriasis, you will first be treated with other medicines or treatment such as phototherapy. If these medicines or treatments do not work well enough, you will be given Remicade to reduce the signs and symptoms of the disease.

Ulcerative colitis

Ulcerative colitis is an inflammatory disease of the bowel. If you suffer from ulcerative colitis, you will first be treated with other medicines. If these medicines do not work well enough, you will be given Remicade to treat the disease.

Crohn's disease

Crohn's disease is an inflammatory disease of the bowel. If you suffer from Crohn's disease, you will first be treated with other medicines. If these medicines do not work well enough, you will be given Remicade to:

- Treat active Crohn's disease.
- Reduce the number of fistulae between the bowel and the skin that have not been successfully treated with other medicines or surgery.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to infliximab or any of the additional ingredients contained in the medicine. For a list of the additional ingredients, see section 6 "Further Information".
- You are allergic to proteins that come from mice.
- You suffer from tuberculosis or another severe infection, such as pneumonia or sepsis.
- You suffer from moderate to severe heart failure.

Do not use Remicade if you suffer from any of the conditions detailed above. If you are not sure, refer to the doctor before you receive Remicade.

Special warnings regarding use of the medicine

Before treatment with Remicade, tell the doctor if you suffer from the following conditions:

You were treated with Remicade in the past

Tell the doctor if you have received treatment with Remicade in the past and are now starting Remicade treatment again.

If you have had a break in your Remicade treatment of more than 16 weeks, there is a higher risk for allergic reactions when you start the treatment again.

Infections

- Before starting treatment with Remicade, tell the doctor if you suffer from any infection, even if the infection is very mild.
- Before starting treatment with Remicade, tell the doctor if you have ever lived

or traveled in an area where the following infections are common: histoplasmosis, coccidioidomycosis, or blastomycosis. These infections are caused by specific types of fungi that may harm the lungs or other parts of your body.
- You may get infections more easily while under treatment with Remicade. If you are 65 years of age or older, you are at higher risk.
- These infections may be serious and include tuberculosis, infections caused by viruses, fungi, bacteria, or other organisms in the environment, and sepsis that may be life-threatening.

Tell your doctor immediately if you suffer from signs of infection during treatment with Remicade. Signs include fever, cough, flu-like signs, general unwell feeling, red or hot skin, sores or dental problems. Your doctor may recommend temporarily stopping treatment with Remicade.

Tuberculosis
- It is very important that you tell the doctor if you have ever had tuberculosis or if you have been in close contact with someone who has or has had tuberculosis.
- The doctor will test you to see if you have tuberculosis. Cases of tuberculosis have been reported in patients treated with Remicade, even in patients who have already been treated with medicines for tuberculosis. The doctor will record the results of the tests in your Patient Reminder Card.
- If the doctor suspects that you are at risk for tuberculosis, you may be treated with anti-tuberculosis medicines before you start using Remicade.

Report to the doctor immediately if you get signs of tuberculosis during treatment with Remicade. These signs include persistent cough, weight loss, tiredness, fever, night sweats.

Hepatitis B virus
- Before starting treatment with Remicade, tell the doctor if you are a carrier of hepatitis B or if you have ever had it.
- Tell the doctor if you think you might be at risk of contracting hepatitis B.
- The doctor should test you for the presence of hepatitis B.
- Treatment with TNF blockers such as Remicade may result in reactivation of hepatitis B virus in patients who carry this virus, and can be life-threatening in some cases.

Heart problems
- Tell the doctor if you suffer from any heart problems, such as mild heart failure.
- The doctor will want to closely monitor your heart function.

Report to the doctor immediately if you experience new symptoms or worsening of existing symptoms of heart failure during treatment with Remicade. These symptoms include shortness of breath or swelling of the feet.

Cancer and lymphoma

- Before starting treatment with Remicade, tell your doctor 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 suffered from it for a long time may be at higher risk for developing lymphoma.
- Children and adults taking Remicade may be at an increased risk of developing lymphoma or another type of cancer.
- Some patients who received TNF blockers, including Remicade, 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 has usually resulted in death. Almost all patients had also received medicines containing azathioprine or 6-mercaptopurine in addition to the TNF blockers.
- Some patients treated with infliximab have developed certain kinds of skin cancer. If you notice any changes in your skin or growths on the skin during or after the treatment with Remicade, report to the doctor.
- Some women who were treated for rheumatoid arthritis with Remicade developed cervical cancer. For women taking Remicade, including those over 60 years of age, the doctor may recommend being examined regularly for cervical cancer.

Lung diseases or heavy smoking

- Before starting treatment with Remicade, tell your doctor if you suffer from a lung disease called chronic obstructive pulmonary disease (COPD) or if you are a heavy smoker.
- Patients suffering from COPD and patients who are heavy smokers may have a higher risk of developing cancer with Remicade treatment.

Diseases of the nervous system

- Before starting treatment with Remicade, tell your doctor if you are suffering, or have suffered in the past, from problems that affect the nervous system. These problems include multiple sclerosis, Guillain-Barré syndrome, if you suffer from seizures or have been diagnosed with optic neuritis.

Tell the doctor immediately if you develop symptoms of neurological disease during treatment with Remicade. Signs include vision changes, weakness in the arms or legs, numbness or tingling in any part of the body.

Abnormal skin openings (fistulae)

- Before starting treatment with Remicade, tell the doctor if you are suffering from abnormal skin openings (fistulae).

Vaccinations

- Tell the doctor if you have recently had or are due to have a vaccination.
- You should receive recommended vaccinations before starting Remicade treatment. You may receive some vaccines during treatment with Remicade, but you should not receive live vaccines (vaccines that contain a living but weakened infectious agent) while using Remicade, because they may cause

infection.
- If you received Remicade while you were pregnant, your baby may also be at higher risk for getting an infection as a result of receiving a live BCG (Bacillus Calmette-Guérin) vaccine during the first year of life and all other live vaccines during the first 6 months after birth. It is important that you tell your baby's doctors and other healthcare professionals that you used Remicade during pregnancy so they can decide when your baby should receive any vaccine, including live vaccines such as the BCG vaccine (used to prevent tuberculosis).

For more information, see section "Pregnancy, breastfeeding and fertility".

Therapeutic infectious agents
- Talk to the doctor if you have recently received or are scheduled to receive treatment with an infectious agent (such as BCG instillation for the treatment of cancer).

Operations or dental procedures
- Tell your doctor if you are going to undergo any operation or dental procedure.
- Tell the surgeon or dentist that you are being treated with Remicade and show them your "Patient Reminder Card".

Liver problems
- Some patients receiving Remicade have developed serious liver problems.

Tell the doctor straight away if you notice symptoms of liver problems during treatment with Remicade. Symptoms include yellowing of the skin and eyes, dark brown-colored urine, pain or swelling in the upper right side of the area of the abdomen, joint pain, skin rash or fever.

Low blood count
- In some patients receiving Remicade, the body may not make enough of the blood cells that help fight infections or help stop bleeding.

Tell the doctor straight away if you have symptoms of low blood count during treatment with Remicade. Signs include persistent fever, bleeding, a tendency to bruise more easily, small red or purple spots caused by bleeding under the skin or looking pale.

Immune system disorder
- Some patients receiving Remicade have developed symptoms of an immune system disorder called lupus.

Tell the doctor straight away if you develop symptoms of lupus during treatment with Remicade. Signs include joint pain or rash on the cheeks or arms that is sensitive to the sun.

Children and adolescents

The information above also applies to children and adolescents. In addition:
- Some of the children and adolescents who have received TNF blockers such as Remicade developed cancer, including unusual types, which sometimes

resulted in death.
- As compared to adults, more children taking Remicade developed infections.
- Children should be given recommended vaccinations before starting treatment with Remicade.

Children may receive some vaccines during treatment with Remicade, but may not receive live vaccines during the treatment.

If you are not sure whether one or more of the above-described applies to you, speak with the doctor before using Remicade.

Drug interactions

Patients who have inflammatory diseases already take medicines to treat their problems.

These medicines may cause side effects. Your doctor will advise you which other medicines you must keep using during treatment with Remicade.

If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. Especially if you are taking:

Other medicines that you use or have recently used to treat Crohn's disease and ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis or psoriasis, or medicines obtained without a prescription, such as vitamins and herbal medicines.

In particular, tell your doctor if you are using any of the following medicines:
- Medicines that affect the immune system.
- Kineret (anakinra). Do not use Remicade together with Kineret.
- Orencia (abatacept). Do not use Remicade together with Orencia.

While using Remicade, you should not receive live vaccines. If you used Remicade during pregnancy, inform the baby's doctor or other healthcare professionals caring for your baby about your Remicade use before the baby receives any vaccine.

If you are not sure whether the above applies to you, consult with a doctor or pharmacist before using Remicade.

Pregnancy, breastfeeding and fertility
- Consult with a doctor before using Remicade if you are pregnant, breastfeeding, think you are pregnant or are planning pregnancy. Remicade may only be used during pregnancy or breastfeeding if the doctor considers that it is necessary for you.
- You should avoid getting pregnant while using Remicade and for 6 months after stopping the treatment. Consult with the doctor regarding the use of contraception during this time.
- If you received Remicade during pregnancy, your baby may be at higher risk for getting an infection.
- It is important that you tell your baby's doctors and other healthcare

professionals about your Remicade use during pregnancy before your baby receives any vaccine. If you received Remicade while you were pregnant, giving your baby BCG vaccine (used to prevent tuberculosis) within 12 months of birth may result in infection with serious complications, including death. Do not give a live BCG vaccine to your baby within 12 months of birth and do not give any other live vaccines within the first 6 months after birth unless your baby's doctor recommends otherwise. For more information, see section "Vaccinations".

- Severely decreased numbers of white blood cells have been reported in infants born to women who were treated with Remicade during pregnancy. If your baby suffers from continual fever or continual infections, contact your baby's doctor immediately.

Driving and using machinery

It is unlikely that Remicade will affect the ability to drive, use tools or operate machinery. If you feel tired, dizzy or do not feel well after receiving Remicade, do not drive, do not use tools and do not operate machinery.

Important information about some of the ingredients of the medicine

Remicade contains less than 1 mmol sodium (23 mg) per dose, that is to say it is essentially "sodium-free". However, before Remicade is given to you, it is mixed in a solution that contains sodium. Consult with the doctor if you are on a low-sodium diet.

Remicade contains polysorbate 80

This medicine contains 0.50 mg of polysorbate 80 (E433) in each dosage unit, which is equivalent to 0.05 mg/ml. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

3. HOW SHOULD THE MEDICINE BE USED?

Always use the preparation according to the doctor's instructions.
Check with the doctor or pharmacist if you are not sure about the dosage and treatment regimen of the preparation.

- Remicade will be given to you by a doctor or nurse.
- The doctor or nurse will prepare the medicine for injection.
- The solution will be given as an infusion (over two hours) into one of your veins, usually in the arm. After the third treatment, the doctor may decide to give the dose of Remicade over one hour.
- You must remain under medical supervision during administration of Remicade and for one to two hours afterwards.
- The doctor will determine the dosage and the frequency of treatment. This will depend on the illness, weight and the response to Remicade.

Do not exceed the recommended dose.
Do not swallow.
Adhere to the treatment as recommended by the doctor.

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

Use in children:
Remicade may only be given to children for the treatment of Crohn's disease and ulcerative colitis. These children must be 6 years of age or older.

If you received too high a dosage of Remicade:
Since the medicine is given to you by a nurse or doctor, it is not likely that you will receive too high a dosage of the medicine. There are no known side effects associated with administering too much Remicade.

If you forgot or missed a Remicade administration:
If you forgot or missed administration of the medicine at the specified time, make a new appointment as soon as possible.

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 regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Remicade 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 of the side effects are mild to moderate. Some patients may suffer serious side effects and may need treatment. Side effects may occur even after discontinuation of treatment with Remicade.

Refer to the doctor immediately if you notice any of the following:

- **Signs of an allergic reaction:** such as swelling of the face, lips, mouth or throat that may cause difficulty 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. Additional symptoms of an allergic reaction that may occur up to 12 days after receiving the injection include muscle pain, fever, jaw or joint pain, sore throat or headache.
- **Signs of heart problems:** such as chest discomfort or pain, arm pain, abdominal pain, shortness of breath, anxiety, lightheadedness, dizziness, fainting, sweating, nausea, vomiting, fluttering or pounding sensation in your chest, a slow or fast heartbeat, and swelling of your feet.
- **Signs of infection (including tuberculosis):** such as fever, tiredness, cough which may be persistent, shortness of breath, flu-like symptoms, weight loss, night sweats, diarrhea, sores, collection of pus in the gut or around the anus (abscess), dental problems or a burning sensation when passing urine.
- **Possible signs of cancer:** including, but not limited to, swelling of lymph nodes, weight loss, fever, abnormal lumps on the skin, changes in moles or skin coloring, unusual vaginal bleeding.

- **Signs of lung problems:** such as cough, 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 the face, arm or leg, especially on one side of the 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), convulsions, tingling/numbness in various parts of the 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 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:** 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 (sarcoidosis).
- **Signs of low blood count:** such as persistent fever, bleeding or bruising more easily, red or purple spots caused by bleeding under the skin or looking pale.
- **Signs of serious skin problems:** such as red target-like spots or circular patches often with central blisters on the trunk, large areas of peeling 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 your doctor straight away if you notice any of the effects listed above.
The following side effects have been observed with Remicade:

Very common side effects – may affect more than 1 in 10 users:

- Abdominal pain, nausea
- Viral infection, such as herpes or flu
- Upper respiratory tract infections, such as sinusitis
- Headache
- Side effects due to the infusion
- Pain

Common side effects – may affect up to 1 in 10 users:

- Changes in liver function, increase in liver enzymes (diagnosed in blood tests)
- Lung or chest infection, such as bronchitis or pneumonia
- Difficulty breathing or pain when breathing, chest pain
- Bleeding in the stomach or intestines, diarrhea, digestive problems, heartburn, constipation
- Hives, itchy rash or dry skin
- Problems with balance or feeling dizzy

- Fever, increased sweating
- Blood flow problems, such as low or high blood pressure
- Bruising, hot flashes or nosebleed, warm and red skin (flushing)
- Feeling tired or weak
- Bacterial infection, such as sepsis, abscess or skin infection (cellulitis)
- Infection of the skin caused by fungi
- Blood problems, such as anemia or low white blood cell count
- Swelling of the lymph nodes
- Depression, sleep problems
- Eye problems, including red eyes and infections
- Rapid heartbeat (tachycardia) or palpitations
- Joint, muscle or back pain
- Urinary tract infection
- Psoriasis, skin problems, such as eczema and hair loss
- Reactions at the injection site, such as pain, swelling, redness or itching
- Chills, accumulation of fluids under the skin causing swelling
- Feeling numb or having a tingling feeling

Uncommon side effects – may affect up to 1 in 100 users:

- Shortage of blood supply, swelling of the veins
- Accumulation of blood outside of the blood vessels (hematoma) or bruising
- Skin problems such as blisters, warts, abnormal skin coloration or pigmentation, or swollen lips, or thickening of the skin, or red, scaly, and flaky skin
- Severe allergic reactions (anaphylaxis), an immune system disorder called lupus, allergic reaction to foreign proteins
- Prolonged wound healing time
- Swelling of the liver (hepatitis) or gallbladder, liver damage
- Absentmindedness, irritability, confusion, nervousness
- Eye problems including blurred vision, reduced vision, puffy eyes or a stye
- New heart failure or worsening of existing heart failure, slow heart rate
- Fainting
- Convulsions, neurological problems
- Hole in the bowel or blockage of the intestine, abdominal pain or cramps
- Swelling of the pancreas (pancreatitis)
- Fungal infections, such as Candida or fungal infection of the nails
- Lung problems (such as edema)
- Accumulation of fluid around the lung (pleural effusion)
- Narrowed airway in the lungs causing breathing difficulties
- Inflamed lining of the lung, causing sharp chest pain that feels worse with breathing (pleurisy)
- Tuberculosis
- Kidney infections
- Low platelet count, too many white blood cells

- Vaginal infections
- Blood test results showing autoantibodies
- Changes in cholesterol and fat levels in the blood
- Weight gain (for most patients, the weight gain was small)

Rare side effects – may affect up to 1 in 1,000 users:

- A type of blood cancer (lymphoma)
- Deficient or reduced oxygen supply to the body via the blood circulation, circulation problems, such as narrowing of blood vessels
- Meningitis
- Infection due to weakening of the immune system
- Hepatitis B infection, if you have had such an inflammation in the past
- Inflamed liver caused by a problem with the immune system (autoimmune hepatitis)
- Liver problem that causes yellowing of the skin or eyes (jaundice)
- Unusual 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)
- Problems of the immune system that could affect the lungs, skin and lymph nodes (such as sarcoidosis)
- Collections of immune cells resulting from an inflammatory response (granulomatous lesions)
- Apathy
- Severe skin problems, such as toxic epidermal necrolysis, Stevens-Johnson syndrome and acute generalized exanthematous pustulosis
- Other skin problems, such as erythema multiforme, lichenoid reactions (itchy reddish-purple skin rash and/or threadlike white-gray lines on mucous membranes), blisters and peeling skin, or boils (furunculosis)
- Serious nervous system problems, such as transverse myelitis, multiple sclerosis-like disease, optic neuritis and Guillain-Barré syndrome
- Inflammation in the eye that may cause changes in 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
- 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

Side effects of unknown frequency – frequency cannot be estimated from the available data:

- Cancer in children and adults

- A rare blood cancer that occurs mainly in teenage boys or young men (hepatosplenic T-cell lymphoma)
- Liver failure
- Merkel cell carcinoma (a type of skin cancer)
- Kaposi's sarcoma, a rare type of cancer related to infection with the human herpes virus 8. Kaposi's sarcoma most commonly manifests as purple lesions on the skin.
- Worsening of a condition called dermatomyositis (seen as a skin rash accompanied by muscle weakness)
- Heart attack
- Stroke
- Temporary loss of sight during or within 2 hours of infusion
- Infection due to a live vaccine because of a weakened immune system
- Problems following a medical procedure (including infectious and non-infectious problems)

Additional side effects in children and adolescents

In children who took Remicade for treatment of Crohn's disease, some differences were seen in side effects as compared to adults who took Remicade for Crohn's disease. The side effects that occurred more in children are: low overall levels of red blood cells (anemia), blood in the stool, low overall level of white blood cells (leukopenia), redness or flushing, viral infections, low levels of white blood cells that fight infections (neutropenia), bone fractures, bacterial infections, allergic reactions of the breathing tracts.

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

Reporting 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 the link:
https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

- Remicade will generally be stored by healthcare professionals in a hospital or clinic.
- Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C-8°C).
- This medicine can also be stored in the original carton outside of refrigerated

storage up to a maximum of 25°C for a single period of up to 6 months, but not beyond the original expiry date. In this situation, do not return to refrigerated storage again. Write the date of removal from the refrigerator on the carton including day/month/year. Discard this medicine if not used within 6 months from the date of removal from the refrigerator or the expiry date printed on the carton, whichever is earlier.

- It is recommended that when Remicade is prepared for infusion, it is used as soon as possible (within 3 hours of preparation). If the solution was prepared in a germ-free environment, it can be kept in the refrigerator (2°C-8°C) for 24 hours.
- Do not use the solution if it is discolored or if there are particles in it.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:
Sucrose, sodium phosphate dibasic dihydrate, sodium phosphate monobasic monohydrate, polysorbate 80

What the medicine looks like and the contents of the package:
Remicade is supplied in a glass vial containing a powder for preparation of concentrate for solution for infusion. The powder is in the form of freeze-dried white pellets.
There is one vial in each package.

Manufacturer: Janssen Biologics B.V., Einsteinweg 101, 233, Leiden, Netherlands.

Registration Holder: J-C Health Care Ltd., Kibbutz Shefayim, 6099000, Israel.

Revised in April 2025.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:
137-18-29865-05.

Instructions for use and handling – reconstitution, dilution and administration

1. Calculate the dose and the number of Remicade vials needed. Each Remicade vial contains 100 mg infliximab. Calculate the total volume of reconstituted Remicade solution required.
2. Under aseptic conditions, reconstitute each Remicade vial with 10 ml of water for injections, using a syringe equipped with a 21-gauge (0.8 mm) or smaller needle. Remove flip-top from the vial and wipe the top with a 70% alcohol swab. Insert the syringe needle into the vial through the centre of the rubber stopper and direct the stream of water for injections to the glass wall of the vial. Gently swirl the solution by rotating the vial to dissolve the lyophilised powder. Avoid prolonged or vigorous agitation. DO NOT SHAKE. Foaming of the solution on reconstitution is not unusual. Allow the reconstituted solution to stand for 5 minutes. Check that the solution is

colourless to light yellow and opalescent. The solution may develop a few fine translucent particles, as infliximab is a protein. Do not use if opaque particles, discolouration, or other foreign particles are present.

3. Dilute the total volume of the reconstituted Remicade solution dose to 250 ml with sodium chloride 9 mg/ml (0.9%) solution for infusion. Do not dilute the reconstituted Remicade solution with any other diluent. The dilution can be accomplished by withdrawing a volume of the sodium chloride 9 mg/ml (0.9%) solution for infusion from the 250 ml glass bottle or infusion bag equal to the volume of reconstituted Remicade. Slowly add the total volume of reconstituted Remicade solution to the 250 ml infusion bottle or bag. Gently mix. For volumes greater than 250 ml, either use a larger infusion bag (e.g., 500 ml, 1000 ml) or use multiple 250 ml infusion bags to ensure that the concentration of the infusion solution does not exceed 4 mg/ml.
4. Administer the infusion solution over a period of not less than the infusion time recommended (see section 4.2). Use only an infusion set with an in-line, sterile, non-pyrogenic, low protein-binding filter (pore size 1.2 micrometer or less). Since no preservative is present, it is recommended that the administration of the solution for infusion is to be started as soon as possible and within 3 hours of reconstitution and dilution. When reconstitution and dilution are performed under aseptic conditions, Remicade infusion solution can be used within 24 hours if stored at 2°C to 8°C. Do not store any unused portion of the infusion solution for reuse.
5. No physical biochemical compatibility studies have been conducted to evaluate the co-administration of Remicade with other agents. Do not infuse Remicade concomitantly in the same intravenous line with other agents.
6. Visually inspect Remicade for particulate matter or discolouration prior to administration. Do not use if visibly opaque particles, discolouration or foreign particles are observed.
7. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.