Package leaflet: Information for the user

Remsima 120 mg solution for injection in pre-filled syringe
Infliximab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- Your doctor will also give you a Patient Alert Card, which contains important safety information you need to be aware of before and during your treatment with Remsima.
- When starting a new card, keep this card as a reference for 4 months after your last dose of Remsima.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Remsima is and what it is used for

Remsima 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 (tumour necrosis factor) alpha.

Remsima belongs to a group of medicines called 'TNF blockers'. It is used in adults for the following inflammatory diseases:
- Rheumatoid arthritis
- Psoriasis
- Ankylosing spondylitis
- Psoriatic arthritis
- Crohn's disease
- Ulcerative colitis

Remsima works by selectively attaching to TNF alpha and blocking its action. TNF alpha is involved in inflammatory processes of the body so blocking it can reduce the inflammation in your body.

Rheumatoid arthritis
Rheumatoid arthritis is an inflammatory disease of the joints. If you have active rheumatoid arthritis you will first be given other medicines. If these medicines do not work well enough, you will be given Remsima which you will take with another medicine called methotrexate to:
- reduce the signs and symptoms of your disease,
- slow down the damage in your joints,
- improve your physical function.

Psoriatic arthritis

Psoriatic arthritis is an inflammatory disease of the joints, usually accompanied by psoriasis. If you have active psoriatic arthritis you will first be given other medicines. If these medicines do not work well enough, you will be given Remsima to:
- reduce the signs and symptoms of your disease,
- slow down the damage in your joints,
- improve your physical function.

Ankylosing spondylitis (Bechterew's disease)
Ankylosing spondylitis is an inflammatory disease of the spine. If you have ankylosing spondylitis you will first be given other medicines. If these medicines do not work well enough, you will be given Remsima to:
- reduce the signs and symptoms of your disease,
- improve your physical function.

Psoriasis
Psoriasis is an inflammatory disease of the skin. If you have moderate to severe plaque psoriasis, you will first be given other medicines or treatments, such as phototherapy. If these medicines or treatments do not work well enough, you will be given Remsima to reduce the signs and symptoms of your disease.

Ulcerative colitis
Ulcerative colitis is an inflammatory disease of the bowel. If you have ulcerative colitis you will first be given other medicines. If these medicines do not work well enough, you will be given Remsima to treat your disease.

Crohn's disease
Crohn's disease is an inflammatory disease of the bowel. If you have Crohn's disease you will first be given other medicines. If these medicines do not work well enough, you will be given Remsima to:
- treat active Crohn's disease,
- reduce the number of abnormal openings (fistulae) between your bowel and your skin that have not been controlled by other medicines or surgery.

2. What you need to know before you use

Remsima You must not use Remsima if
- you are allergic to infliximab or any of the other ingredients of this medicine (listed in section 6),
- you are allergic to proteins that come from mice,
- you have tuberculosis (TB) or another serious infection such as pneumonia or sepsis (serious bacterial infection of the blood),
- you have heart failure that is moderate or severe.

Do not use Remsima if any of the above applies to you. If you are not sure, talk to your doctor before you are given Remsima.

Warnings and precautions
Talk to your doctor before using Remsima, if you have:

<u>Had treatment with any medicine containing infliximab before</u>

- Tell your doctor if you have had treatment with medicines containing infliximab in the past and are now starting Remsima treatment again.
- If you have had a break in your treatment with infliximab of more than 16 weeks, there is a higher risk for allergic reactions when you start the treatment again.

<u>Local injection site reactions</u>

- Some patients receiving iniximab via injection under the skin 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

- Tell your doctor before you are given Remsima if you have an infection even if it is a very minor one.
- Tell your doctor before you are given Remsima if you have ever lived in or travelled to an area where infections called histoplasmosis, coccidioidomycosis, or blastomycosis are common. These infections are caused by specific types of fungi that can affect the lungs or other parts of your body.
- You may get infections more easily when you are being treated with Remsima. If you are 65 years of age or older, you have a greater 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 straight away if you get signs of infection during treatment with Remsima. Signs include fever, cough, flu-like signs, feeling unwell, red or hot skin, wounds or dental problems. Your doctor may recommend temporarily stopping Remsima.

Tuberculosis (TB)

- It is very important that you tell your doctor if you have ever had TB or if you have been in close contact with someone who has had or has TB.
- Your doctor 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 doctor will record these tests on your Patient Alert Card.
- If your doctor feels that you are at risk for TB, you may be treated with medicines for TB before you are given Remsima.

Tell your doctor straight away if you get signs of TB during treatment with Remsima. Signs include persistent cough, weight loss, feeling tired, fever, night sweats.

Hepatitis B virus

- Tell your doctor before you are using Remsima 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 hepatitis B.
- Your doctor should test you for hepatitis B virus.
- Treatment with TNF blockers such as Remsima 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 and may give you medicines such as effective antiviral therapy with supportive treatment.

Heart probelms

- Tell your doctor if you have any heart problems, such as mild heart failure.
- Your doctor will want to closely monitor your heart.

Tell your doctor straight away if you get new or worsening signs of heart failure during treatment with Remsima. Signs include shortness of breath or swelling of your feet.

Cancer and lymphoma

- Tell your doctor before you are given Remsima if you have or have ever had lymphoma (a type of blood cancer) or any other cancer.
- Patients with severe rheumatoid arthritis, who have had the disease for a long time, may be at

higher risk of developing lymphoma.

- Patients taking Remsima may have an increased risk of developing lymphoma or another cancer.
- Some patients who have received TNF-blockers, including iniximab 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 mercaptopurine in addition to TNF-blockers.
- Some patients treated with iniximab have developed certain kinds of skin cancer. If there are any changes in your skin or growths on the skin during or after therapy, tell your doctor.
- Some women being treated for rheumatoid arthritis with iniximab have developed cervical cancer. For women taking Remsima including those over 60 years of age, your doctor may recommend regular screening for cervical cancer.

Lung disease or heavy smoking

- Tell your doctor before you are given Remsima 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 have a higher risk of developing cancer with Remsima treatment.

Nervous system disease

- Tell your doctor before you are given Remsima if you have or have ever had a problem that affects your nervous system. This includes multiple sclerosis, Guillain-Barré syndrome, if you have fits or have been diagnosed with 'optic neuritis'.

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

Abnormal skin openings

- Tell your doctor if you have any abnormal skin openings (fistulae) before you are given Remsima.

Vaccinations

- Talk to your doctor if you recently have had or are due to have a vaccine.
- You should receive recommended vaccinations before starting Remsima treatment. You may receive some vaccines during treatment with Remsima but you should not receive live vaccines (vaccines that contain a living but weakened infectious agent) while using Remsima because they may cause infections.
- If you received Remsima while you were pregnant, your baby may also be at higher risk for getting an infection with live vaccines for up to six months after birth. It is important that you tell your baby's doctors and other health care professionals about your Remsima use so they can decide when your baby should receive any vaccine, including live vaccines such as BCG (used to prevent tuberculosis). For more information see section on Pregnancy and breast-feeding.

Therapeutic infectious agents

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

Operations or dental procedures

- Tell your doctor if you are going to have any operations or dental procedures.
- Tell your surgeon or dentist that you are having treatment with Remsima by showing them your

Patient Alert Card.

Liver problems

- Some patients receiving infliximab have developed serious liver problems.
- Tell your doctor if you experience jaundice (skin and eyes turning yellow), dark brown-coloured urine, extreme tiredness (severe fatigue) or pain on the right side of your stomach area (right-sided abdominal pain).

Low blood counts

- In some patients receiving iniximab, the body may not make enough of the blood cells that help fight infections or help stop bleeding.
- Tell your doctor straight away if you get symptoms of low blood counts during treatment with Remsima. 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 iniximab 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. Signs include joint pain or a rash on cheeks or arms that is sensitive to the sun.

Children and adolescents
Do not give this medicine to children and adolescents under 18 years of age because there are no data that show that this medicine is safe and works in this age group.

Other medicines and Remsima
Patients who have inflammatory diseases already take medicines to treat their problem. These medicines may cause side effects. Your doctor will advise you what other medicines you must keep using while you are having Remsima.

Tell your doctor if you are using, have recently used or might use any other medicines, including any other medicines to treat 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 your immune system.
- Kineret (which contains anakinra). Remsima and Kineret should not be used together.
- Orencia (which contains abatacept). Remsima and Orencia should not be used together.

While using Remsima you should not receive live vaccines. If you were using Remsima during pregnancy, tell your baby's doctor and other health care professionals caring for your baby about your Remsima use before the baby receives any vaccines.

If you are not sure if any of the above applies to you, talk to your doctor, pharmacist or nurse before using Remsima.

Pregnancy, breast-feeding and fertility
- If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. Remsima should only be used during pregnancy if your doctor feels it is necessary for you.

- You should avoid getting pregnant when you are being treated with Remsima and for 6 months after you stop being treated with it. Discuss the use of contraception during this time with your doctor.
- Do not breast-feed when you are being treated with Remsima or for 6 months after your last treatment with Remsima.
- If you received Remsima during your pregnancy, your baby may have a higher risk for getting an infection.
- It is important that you tell your baby's doctors and other healthcare professionals about your Remsima use before your baby is given any vaccine. If you received Remsima 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 section on vaccination.
- 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 fevers or infections, contact your baby's doctor immediately.

Driving and using machines
Remsima is not likely to affect your ability to drive or use tools or machines. If you feel tired, dizzy, or unwell after having Remsima, do not drive or use any tools or machines.

Remsima contains Sorbitol
Sorbitol is a source of fructose. If your doctor has told you that you have an intolerance to some sugars or if you have been diagnosed with hereditary fructose intolerance (HFI), a rare genetic disorder in which a person cannot break down fructose, talk to your doctor before you take or receive this medicine.

3. How to use Remsima

Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

Rheumatoid arthritis
Your doctor will start your treatment with or without two Remsima intravenous infusion doses of 3 mg for every kg of body weight (given to you into a vein, usually in your arm, over a period of 2 hours). If Remsima intravenous infusion doses are given to start the treatment, they are administered 2 weeks apart via intravenous infusion. After 4 weeks from the last intravenous infusion, you will be given Remsima via injection under the skin (subcutaneous injection).
The usual recommended dose of Remsima subcutaneous injection is 120 mg once every 2 weeks regardless of weight.

Psoriatic arthritis, ankylosing spondylitis (Bechterew's disease) and psoriasis
Your doctor will start your treatment with two Remsima doses of 5 mg for every kg of body weight administered 2 weeks apart via intravenous infusion (given to you into a vein, usually in your arm, over a period of 2 hours). The first subcutaneous injection (injection under the skin) of Remsima will be given after 4 weeks from the last intravenous infusion. The usual recommended dose of Remsima administered subcutaneously is 120 mg once every 2 weeks if your body weight is below 80 kg or 240 mg (two injections of Remsima 120 mg) once every 2 weeks if your body weight is at or above 80 kg.

How Remsima is given
- Remsima 120 mg 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.
- For patients with rheumatoid arthritis, your doctor may start your Remsima treatment with or without two Remsima intravenous infusion doses. For patients with Crohn's disease, ulcerative colitis, ankylosing spondylitis, psoriatic arthritis or psoriasis, two Remsima infusion doses will be given to start your Remsima treatment.

If Remsima treatment is initiated without two Remsima intravenous infusion doses, the table below shows how often you will usually have this medicine after your first dose.

2nd dose	1 week after your 1st dose
3rd dose	2 weeks after your 1st dose
4th dose	3 weeks after your 1st dose
5th dose	4 weeks after your 1st dose
Further doses	6 weeks after your 1st dose and every 2 weeks thereafter

- If two Remsima intravenous infusion doses are given by your doctor or nurse to start the treatment, they will be given 2 weeks apart and the first Remsima subcutaneous injection will be given 4 weeks after the last intravenous infusion followed by Remsima subcutaneous injections given every 2 weeks.
- The first subcutaneous injection of Remsima will be administered under the supervision of your doctor.
- After proper training, if you feel you are well-trained and confident to inject Remsima yourself, your doctor may allow you to inject subsequent doses of Remsima yourself at home.
- Talk to your doctor 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 use more Remsima than you should
If you have used more Remsima than you should (either by injecting too much on a single occasion or by using it too frequently), talk to a doctor, pharmacist or nurse immediately. Always have the outer carton of the medicine with you, even if it is empty.

If you forget to use Remsima

Missed dose for up to 7 days
If you miss a dose of Remsima for up to 7 days, after the original scheduled dose, you should take the missed dose immediately. Take your next dose on the next originally planned date and thereafter bi-weekly.

Missed dose for 8 days or more
If you miss a dose of Remsima for 8 days or more, after the original scheduled dose, you should not take the missed dose. Take your next dose on the next originally planned date and thereafter bi-weekly.
If you are not sure when to inject Remsima, call your doctor.
If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets 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 your treatment with Remsima has stopped.

Tell your doctor straight away if you notice any of the following:
- **Signs of an allergic reaction** such as swelling of your face, lips, mouth or throat which may cause difficulty in swallowing or breathing, skin rash, hives, swelling of the hands, feet or ankles. An allergic reaction could happen within 2 hours of your injection or later. Other 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 a heart problem** such as chest discomfort or pain, arm pain, stomach pain, shortness of breath, anxiety, lightheadedness, dizziness, fainting, sweating, nausea (feeling sick), vomiting, fluttering or pounding in your chest, a fast or a slow heartbeat, and swelling of your feet
- **Signs of infection (including TB)** such as fever, feeling tired, cough which may be

persistent, shortness of breath, flu-like symptoms, weight loss, night sweats, diarrhoea, wounds, 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 colouring, or unusual vaginal bleeding.
- **Signs of a lung problem** such as coughing, breathing difficulties or tightness in the chest.
- **Signs of a nervous system problem (including eye problems)** such as signs of a stroke (sudden numbness or weakness of your face, arm or leg, 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/numbness in any part of your body, or weakness in arms or legs, changes in eyesightsuch as double vision or other eye problems.
- **Signs of a liver problem** (including hepatitis B infection when you have had hepatitis B in the past) such as yellowing of the skin or eyes, dark-brown coloured urine or pain or swelling in the upper right side of the stomach area, joint pain, skin rashes, 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 a low blood count** 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 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 above.

The following side effects have been observed with Remsima:

Very common (may affect more than 1 in 10 people)
- Stomach pain, feeling sick
- Viral infections such as herpes or flu
- Upper respiratory infections such as sinusitis
- Headache
- Side effect due to an injection
- Pain.

Common (may affect up to 1 in 10 people)
- Changes in how your liver works, increase in liver enzymes (shown in blood tests)
- Lung or chest infections such as bronchitis or pneumonia
- Fungal infection of the skin
- Difficult or painful breathing, chest pain
- Bleeding in the stomach or intestines, diarrhoea, indigestion, heartburn, constipation
- Nettle-type rash (hives), itchy rash or dry skin
- Balance problems or feeling dizzy
- Fever, increased sweating
- Circulation problems such as low or high blood pressure
- Bruising, hot flush or nosebleed, warm, red skin (flushing)
- Feeling tired or weak
- Bacterial infections such as blood poisoning, abscess or infection of the skin (cellulitis)
- Blood problems such as anaemia or low white blood cell count
- Swollen lymph nodes
- Depression, problems sleeping
- 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 or itching
- Chills, a build-up of fluid under the skin causing swelling
- Feeling numb or having a tingling feeling.

Uncommon (may affect 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 swollen lips, or thickening of the skin, or red, scaly, and flaky skin
- Severe allergic reactions (e.g. anaphylaxis), an immune system disorder called lupus, allergic reactions to foreign proteins
- Wounds taking longer to heal
- 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 sties
- New or worsening heart failure, slow heart rate
- Fainting
- Convulsions, nerve problems
- A hole in the bowel or blockage of the intestine, stomach pain or cramps
- Swelling of your pancreas (pancreatitis)
- Fungal infections such as yeast infection, including fungal infection of the nails
- Lung problems (such as oedema)
- 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)
- Tuberculosis
- Kidney infections
- Low platelet count, too many white blood cells
- Infections of the vagina
- Blood test result showing 'antibodies' against your own body
- Changes in cholesterol and fat levels in the blood

Rare (may affect up to 1 in 1,000 people)
- A type of blood cancer (lymphoma)
- Your blood not supplying enough oxygen to your body, circulation problems such as narrowing of a blood vessel
- Inflammation of the lining of the brain (meningitis)
- Infections due to a weakened immune system
- Hepatitis B infection when you have had hepatitis B in the past
- Inflammation of liver due to immune system attacking the liver
- 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 disorders that could affect the lungs, skin and lymph nodes (such as sarcoidosis)
- Collections of immune 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 acutegeneralised 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 counts, including a severely decreased number of white blood cells.
- Small red or purple spots caused by bleeding into 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).

Not known (frequency cannot be estimated from the available data)
- Cancer in children and adults
- A rare blood cancer affecting mostly young males (hepatosplenic T-cell lymphoma)
- Liver failure
- Merkel cell carcinoma (a type of skin cancer)
- Worsening of a condition called dermatomyositis (seen as a skin rash accompanying muscle weakness)
- Heart attack
- Stroke
- Temporary loss of sight during or within 2 hours of injection
- Infection due to weakened immune system following use of live vaccines

5. How to store Remsima

The storage details should you need them are as follows:

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the label and the carton after "EXP". The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C - 8°C). Do not freeze. Keep the medicinal product in its outer carton to protect from light.
- 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 14 days, but not beyond the original expiry date. In this situation, do not return to refrigerated storage again. Write the new expiry date on the carton including day/month/year. Discard this medicine if not used by the new expiry date or the expiry date printed on the carton, whichever is earlier.
- Do not use this medicine if you notice that the liquid is different to clear colourless or pale brown or see any particles present.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Remsima contains
- The active substance is infliximab. Each pre-filled syringe contains 120 mg/mL of infliximab.
- The other ingredients are acetic acid, sodium acetate trihydrate, sorbitol, polysorbate 80 and water for injection.

What Remsima looks like and contents of the pack
Remsima is clear to opalescent, colourless to pale brown solution which is supplied as a single use pre-filled syringe.
Each pack contains 2 pre-filled pens with 2 alcohol pads.

Product License Holder
CELLTRION HEALTHCARE SINGAPORE
PRIVATE LIMITED
8 CROSS STREET
#10-00 PWC BUILDING
SINGAPORE (048424)

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

This leaflet was last revised in May 2023

7. Instructions for use

Remsima (established name)

Single-Use Pre-Filled Syringe for Subcutaneous Injection
120 mg/1.0 mL

Read carefully these instructions before using the Remsima Syringe. Consult your healthcare provider if you have questions about using the Remsima Syringe.

Important information

- Use the Syringe **ONLY if** your healthcare provider has trained you on the right way to prepare for and to give an injection.
- Ask your healthcare provider how often you will need to give an injection.
- Rotate the injection site each time you give an injection. Each new injection site should be at least 3 cm away from the previous injection site.

⚠ **Warning! Do not** use the Syringe if it has been dropped or is visibly damaged.
⚠ **Warning! Do not** reuse the Syringe.
⚠ **Warning! Do not** shake the Syringe at any time.

About the Remsima Syringe

Parts of the Syringe (see *Figure A*):

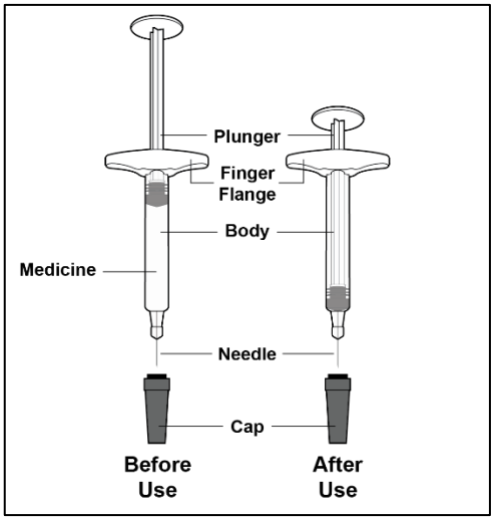

Figure A

⚠ **Caution! Do not** remove the Cap until you are ready to inject. Once you remove the Cap, **do not** recap the Syringe.

How to store the Syringe

- Store the Syringe in a refrigerator at 2°C to 8ºC.
- Keep the Syringe in the original carton to protect it from light.

⚠ **Warning! Do not** freeze the Syringe. If the Syringe has been frozen, **do not** use the Syringe even if it is thawed.
⚠ **Warning! Do not** warm the Syringe using heat sources such as hot water or a microwave. Let the Syringe naturally warm at room temperature for 30 minutes before giving an injection.

- You may store the Syringe at room temperature between 20°C to 25°C for up to 14 days.
- Once the Syringe has reached room temperature, **do not** put it back in the refrigerator.

- Keep the Syringe and injection supplies out of the sight and reach of children.

Prepare for the injection

1. Gather the supplies for the injection.

a. Prepare a clean, flat surface, such as a table or countertop, in a well-lit area.
b. Remove the Syringe from the carton by holding the middle of the Syringe Body.
c. Ensure you have the following supplies:
- Syringe
- Alcohol swab
- Cotton ball or gauze*
- Adhesive bandage*
- Sharps disposal container*

**Items not included in the carton.*

2. Inspect the Syringe.

a. Look at the Syringe and confirm that it does not show signs of damage and that the expiration date has not passed (see *Figure B*).

⚠ **Warning! Do not** use the Syringe if:
- It is cracked or damaged.
- The expiration date has passed.

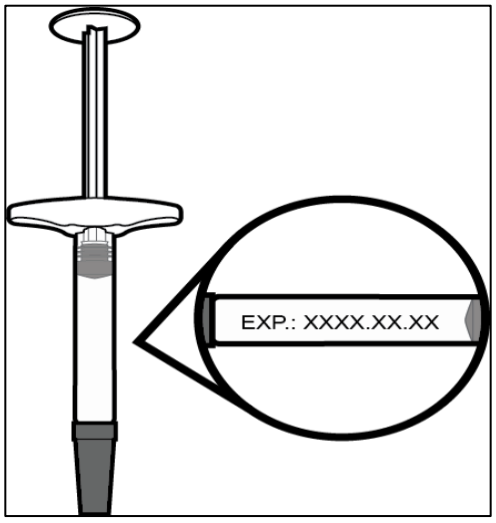

Figure B

3. Inspect the Medicine.

a. Look at the Body and confirm that the liquid is clear and colourless or pale brown (see *Figure C*).

⚠ **Warning! Do not** use the Syringe if the liquid is different to clear colourless or pale brown or contains particles in it.

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

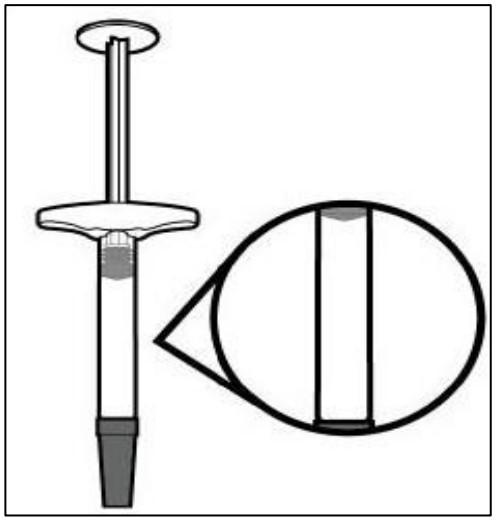

Figure C

4. Wait 30 minutes.

a. Leave the Syringe at room temperature for 30 minutes to allow it to naturally warm up (see *Figure D*).

⚠ **Warning! Do not** warm the Syringe using heat sources such as hot water or a microwave.

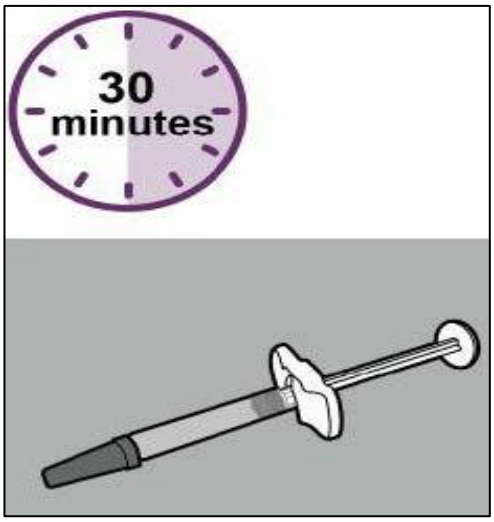

Figure D

5. Choose an injection site (see *Figure E*).

a. Select an injection site. You may inject into:

- The front of the thighs.
- The abdomen except for the 5 cm around the belly button (navel).
- The outer area of the upper arms (caregiver ONLY).

⚠ **Warning! Do not** inject into skin that is within 5 cm of your belly button (navel), or is tender, damaged, bruised, or scarred.

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

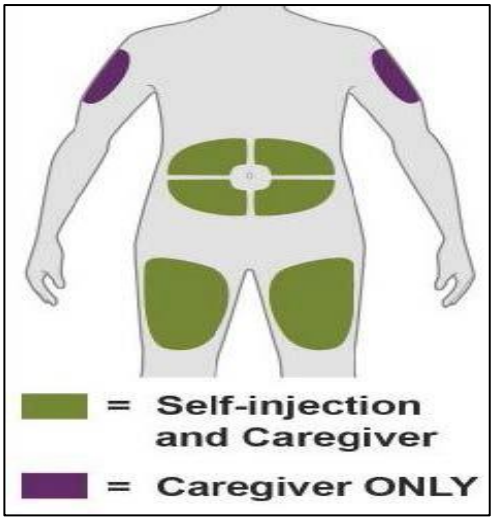

Figure E

6. Wash your hands.

a. Wash your hands with soap and water and dry them thoroughly (see *Figure F*).

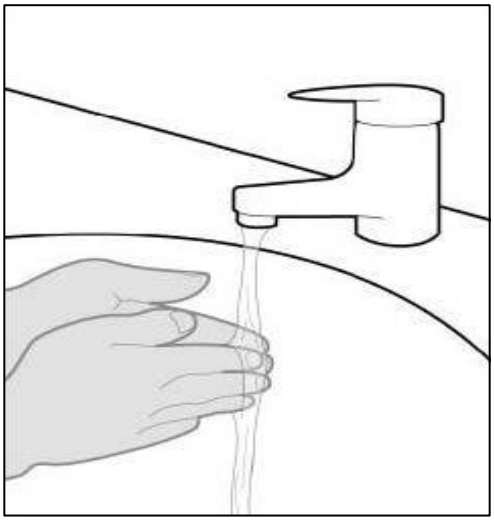

Figure F

7. Clean the injection site.

a. Clean the injection site with an alcohol swab (see *Figure G*).
b. Let the skin dry before injecting.

⚠ **Warning! Do not** blow on or touch the injection site again before giving the injection.

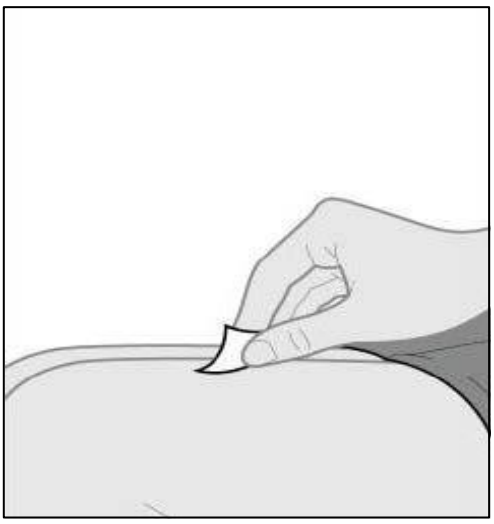

Figure G

Give the injection

8. Remove the Cap.

a. Pull the Cap straight off and set it aside (see *Figure H*).

⚠ **Warning! Do not** remove the Cap until you are ready to inject.

⚠ **Warning! Do not** try to put the needle cover back onto the Syringe.

⚠ **Warning! Do not** touch the Needle. Doing so may result in a needle stick injury.

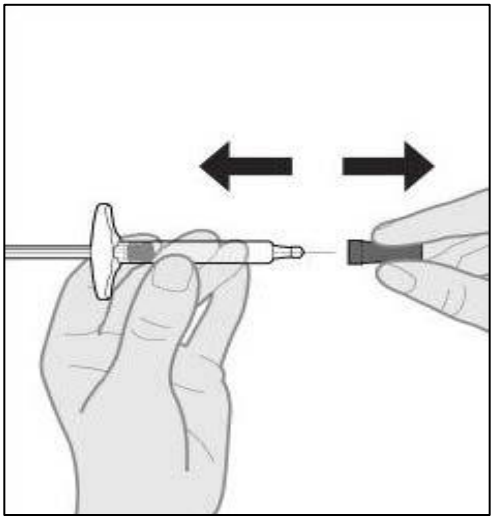

Figure H

9. Insert the Syringe into the injection site.

a. Gently pinch a fold of skin at the injection site with one hand.
b. With a quick and "dart-like" motion, insert the Needle completely into the fold of the skin at a 45-degree angle (see *Figure I*).

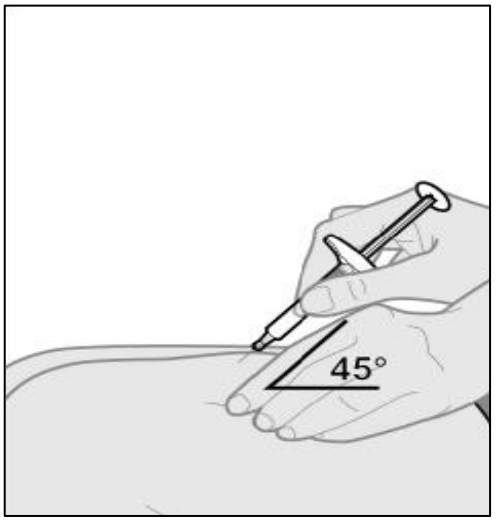

Figure I

10. Give the injection.

a. After the Needle is inserted, release the pinch.
b. Push the Plunger down slowly and as far as it will go until the Syringe is empty (see *Figure J*).

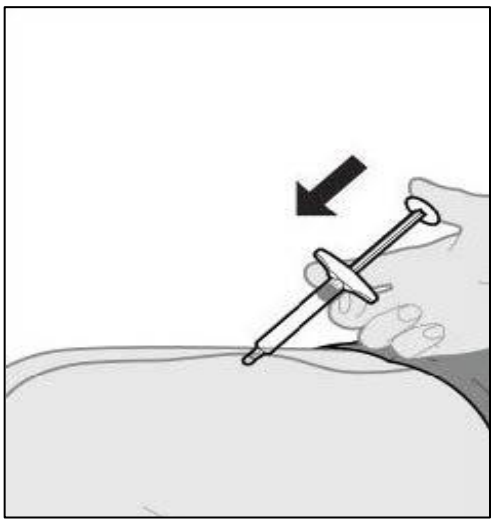

Figure J

11. Remove the Needle from the injection site.

a. Remove the Needle from the skin at the same angle it was inserted (see *Figure K*).

⚠ **Warning! Do not** re-use the Syringe.

⚠ **Warning! Do not** try to put the needle cover back onto the Syringe.

⚠ **Warning! Do not** touch the Needle.

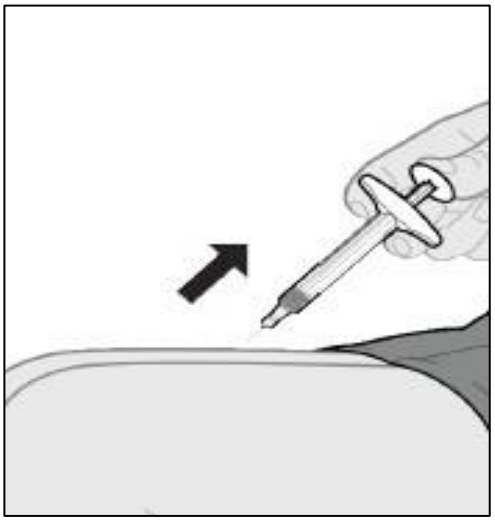

Figure K

After the injection

12. Dispose of the Syringe.

a. Put the used Syringe and Cap in an approved sharps disposal container immediately after use (see *Figure L*).

⚠ **Warning! Do not** throw away (dispose of) the Syringes in your household waste.

If you do not have an approved sharps disposal container, you may use a household container that is:

- made of a heavy-duty plastic;
- able to close with a tight-fitting, puncture-resistant lid, without sharps being able to come out;
- upright and stable during use;
- leak-resistant; and
- properly labelled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, it

Figure L

should be disposed of in accordance with local requirements.

13. Care for the injection site.

a. Treat the injection site by gently pressing a cotton ball or gauze to the site and apply an adhesive bandage, if necessary.

Package leaflet: Information for the user

Remsima 120 mg solution for injection in pre-filled syringe with passive safety guard
Infliximab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- Your doctor will also give you a Patient Alert Card, which contains important safety information you need to be aware of before and during your treatment with Remsima.
- When starting a new card, keep this card as a reference for 4 months after your last dose of Remsima.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Remsima is and what it is used for

Remsima 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 (tumour necrosis factor) alpha.

Remsima belongs to a group of medicines called 'TNF blockers'. It is used in adults for the following inflammatory diseases:
- Rheumatoid arthritis
- Psoriatic arthritis
- Ankylosing spondylitis (Bechterew's disease)
- Psoriasis.

Remsima works by selectively attaching to TNF alpha and blocking its action. TNF alpha is involved in inflammatory processes of the body so blocking it can reduce the inflammation in your body.

Rheumatoid arthritis
Rheumatoid arthritis is an inflammatory disease of the joints. If you have active rheumatoid arthritis you will first be given other medicines. If these medicines do not work well enough, you will be given Remsima which you will take with another medicine called methotrexate to:
- reduce the signs and symptoms of your disease,
- slow down the damage in your joints,
- improve your physical function.

Psoriatic arthritis

Psoriatic arthritis is an inflammatory disease of the joints, usually accompanied by psoriasis. If you have active psoriatic arthritis you will first be given other medicines. If these medicines do not work well enough, you will be given Remsima to:
- reduce the signs and symptoms of your disease,
- slow down the damage in your joints,
- improve your physical function.

Ankylosing spondylitis (Bechterew's disease)
Ankylosing spondylitis is an inflammatory disease of the spine. If you have ankylosing spondylitis you will first be given other medicines. If these medicines do not work well enough, you will be given Remsima to:
- reduce the signs and symptoms of your disease,
- improve your physical function.

Psoriasis
Psoriasis is an inflammatory disease of the skin. If you have moderate to severe plaque psoriasis, you will first be given other medicines or treatments, such as phototherapy. If these medicines or treatments do not work well enough, you will be given Remsima to reduce the signs and symptoms of your disease.

2. What you need to know before you use Remsima

You must not use Remsima if
- you are allergic to infliximab or any of the other ingredients of this medicine (listed in section 6),
- you are allergic to proteins that come from mice,
- you have tuberculosis (TB) or another serious infection such as pneumonia or sepsis (serious bacterial infection of the blood),
- you have heart failure that is moderate or severe.

Do not use Remsima if any of the above applies to you. If you are not sure, talk to your doctor before you are given Remsima.

Warnings and precautions
Talk to your doctor before using Remsima, if you have:

<u>Had treatment with any medicine containing infliximab before</u>

- Tell your doctor if you have had treatment with medicines containing infliximab in the past and are now starting Remsima treatment again.
- If you have had a break in your treatment with infliximab of more than 16 weeks, there is a higher risk for allergic reactions when you start the treatment again.

<u>Allergic reactions</u>

- Some patients receiving infliximab have experienced allergic reactions. Some of these reactions were severe and potentially life-threatening. These reactions can happen while you are getting your Remsima treatment or shortly afterward. Signs of an allergic reaction can include hives (red, raised, itchy patches of skin), high or low blood pressure, difficulty breathing, fever, chest pain, chills or loss of consciousness.
- Tell your doctor straightaway if you experience any of these signs during or within a few hours following your treatment.
- Your doctor may need to stop or pause your treatment and may give you medicines to treat the allergic reaction. Also, for your next injection, your doctor may give you medications such as antihistamine or paracetamol before the injection.

- Also, some patients treated with infliximab have had delayed allergic reactions. The delayed reactions occurred 3 to 12 days after receiving treatment with infliximab. Tell your doctor right away if you have any of these signs of delayed allergic reaction to Remsima including fever, muscle or joint pain, rash, swelling of the face and hands, headache, difficulty swallowing or sore throat.

Infections

- Tell your doctor before you are given Remsima if you have an infection even if it is a very minor one.
- Tell your doctor before you are given Remsima if you have ever lived in or travelled to an area where infections called histoplasmosis, coccidioidomycosis, or blastomycosis are common. These infections are caused by specific types of fungi that can affect the lungs or other parts of your body.
- You may get infections more easily when you are being treated with Remsima. If you are 65 years of age or older, you have a greater 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 straight away if you get signs of infection during treatment with Remsima. Signs include fever, cough, flu-like signs, feeling unwell, red or hot skin, wounds or dental problems. Your doctor may recommend temporarily stopping Remsima.

Tuberculosis (TB)

- It is very important that you tell your doctor if you have ever had TB or if you have been in close contact with someone who has had or has TB.
- Your doctor 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 doctor will record these tests on your Patient Alert Card.
- If your doctor feels that you are at risk for TB, you may be treated with medicines for TB before you are given Remsima.

Tell your doctor straight away if you get signs of TB during treatment with Remsima. Signs include persistent cough, weight loss, feeling tired, fever, night sweats.

Hepatitis B virus

- Tell your doctor before you are using Remsima 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 hepatitis B.
- Your doctor should test you for hepatitis B virus.
- Treatment with TNF blockers such as Remsima 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 and may give you medicines such as effective antiviral therapy with supportive treatment.

Liver problems

- Some patients receiving infliximab have developed serious liver problems.
- Tell your doctor if you experience jaundice (skin and eyes turning yellow), dark brown-coloured urine, extreme tiredness (severe fatigue) or pain on the right side of your stomach area (right-sided abdominal pain).

Lupus-like problems

- Some patients have developed symptoms that are like the symptoms of Lupus.

- If you develop any of the following symptoms, your doctor may decide to stop your treatment with Remsima: chest discomfort or pain that does not go away, joint pain, shortness of breath, rash on the cheeks or arms that gets worse in the sun.

Heart problems

- Tell your doctor if you have any heart problems, such as mild heart failure.
- Your doctor will want to closely monitor your heart.

Tell your doctor straight away if you get new or worsening signs of heart failure during treatment with Remsima. Signs include shortness of breath or swelling of your feet.

Blood problems

- 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 doctor if you have a fever that does not go away, look very pale, bruise or bleed very easily.
- Your doctor may stop Remsima if your blood disorder is significant.

Cancer and lymphoma

- Tell your doctor before you are given Remsima if you have or have ever had lymphoma (a type of blood cancer) or any other cancer.
- Patients with severe rheumatoid arthritis, who have had the disease for a long time, may be at higher risk of developing lymphoma.
- Adults taking Remsima may have an increased risk of developing lymphoma or another 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 has usually resulted in death. Almost all patients had also received medicines containing azathioprine or 6-mercaptopurine in addition to TNF-blockers.
- Some patients treated with infliximab have developed certain kinds of skin cancer. If there are any changes in your skin or growths on the skin during or after therapy, tell your doctor.
- Some women being treated for rheumatoid arthritis with infliximab have developed cervical cancer. For women taking Remsima including those over 60 years of age, your doctor may recommend regular screening for cervical cancer.

Lung disease or heavy smoking

- Tell your doctor before you are given Remsima 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 have a higher risk of developing cancer with Remsima treatment.

Nervous system disease

- Tell your doctor before you are given Remsima if you have or have ever had a problem that affects your nervous system. This includes multiple sclerosis, Guillain-Barré syndrome, if you have fits or have been diagnosed with 'optic neuritis'.

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

Abnormal skin openings

- Tell your doctor if you have any abnormal skin openings (fistulae) before you are given Remsima.

Vaccinations

- Talk to your doctor if you recently have had or are due to have a vaccine.
- You should receive recommended vaccinations before starting Remsima treatment. You may receive some vaccines during treatment with Remsima but you should not receive live vaccines (vaccines that contain a living but weakened infectious agent) while using Remsima because they may cause infections.
- If you received Remsima while you were pregnant, your baby may also be at higher risk for getting an infection with live vaccines for up to six months after birth. It is important that you tell your baby's doctors and other health care professionals about your Remsima use so they can decide when your baby should receive any vaccine, including live vaccines such as BCG (used to prevent tuberculosis). For more information see section on Pregnancy and breast-feeding.

Therapeutic infectious agents

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

Operations or dental procedures

- Tell your doctor if you are going to have any operations or dental procedures.
- Tell your surgeon or dentist that you are having treatment with Remsima by showing them your Patient Alert Card.

Children and adolescents
Remsima is not recommended for subcutaneous administration to children and adolescents under 18 years old. This is because there is no experience of using the medicine in these age groups.

Other medicines and Remsima
Patients who have inflammatory diseases already take medicines to treat their problem. These medicines may cause side effects. Your doctor will advise you what other medicines you must keep using while you are having Remsima.

Tell your doctor if you are using, have recently used or might use any other medicines, including any other medicines to treat 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 your immune system.
- Kineret (which contains anakinra). Remsima and Kineret should not be used together.
- Orencia (which contains abatacept). Remsima and Orencia should not be used together.

While using Remsima you should not receive live vaccines. If you were using Remsima during pregnancy, tell your baby’s doctor and other health care professionals caring for your baby about your Remsima use before the baby receives any vaccines.

If you are not sure if any of the above applies to you, talk to your doctor, pharmacist or nurse before using Remsima.

Pregnancy, breast-feeding and fertility
- If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. Remsima should only be used during pregnancy if your doctor feels it is necessary for you.

- You should avoid getting pregnant when you are being treated with Remsima and for 6 months after you stop being treated with it. Discuss the use of contraception during this time with your doctor.
- Do not breast-feed when you are being treated with Remsima or for 6 months after your last treatment with Remsima.
- If you received Remsima during your pregnancy, your baby may have a higher risk for getting an infection.
- It is important that you tell your baby's doctors and other healthcare professionals about your Remsima use before your baby is given any vaccine. If you received Remsima 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 section on vaccination.
- 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 fevers or infections, contact your baby's doctor immediately.

Driving and using machines
Remsima is not likely to affect your ability to drive or use tools or machines. If you feel tired, dizzy, or unwell after having Remsima, do not drive or use any tools or machines.

Remsima contains Sorbitol
Sorbitol is a source of fructose. If your doctor has told you that you have an intolerance to some sugars or if you have been diagnosed with hereditary fructose intolerance (HFI), a rare genetic disorder in which a person cannot break down fructose, talk to your doctor before you take or receive this medicine.

3. How to use Remsima

Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

Rheumatoid arthritis
Your doctor will start your treatment with two Remsima doses of 3 mg for every kg of body weight administered 2 weeks apart via intravenous infusion (given to you into a vein, usually in your arm, over a period of 2 hours). The first subcutaneous injection (injection under the skin) of Remsima will be given after 4 weeks from the last intravenous infusion. The usual recommended dose of Remsima administered subcutaneously is 120 mg once every 2 weeks regardless of weight.

Psoriatic arthritis, ankylosing spondylitis (Bechterew's disease) and psoriasis
Your doctor will start your treatment with two Remsima doses of 5 mg for every kg of body weight administered 2 weeks apart via intravenous infusion (given to you into a vein, usually in your arm, over a period of 2 hours). The first subcutaneous injection (injection under the skin) of Remsima will be given after 4 weeks from the last intravenous infusion. The usual recommended dose of Remsima administered subcutaneously is 120 mg once every 2 weeks if your body weight is below 80 kg or 240 mg (two injections of Remsima 120 mg) once every 2 weeks if your body weight is at or above 80 kg.

How Remsima is given
- It is important to check the product labels to ensure that the correct formulation is being given as prescribed. Remsima 120 mg is designed only for subcutaneous administration and is not for intravenous use.
- The first two Remsima intravenous infusions will be given to you by your doctor or nurse.
- At the two Remsima treatment via intravenous infusions, your doctor or nurse may inject Remsima subcutaneously. However, you and your doctor may decide that you can inject Remsima yourself. In this case, you will get training on how to inject Remsima yourself.

- Talk to your doctor if you have any questions about giving yourself an injection. You will find detailed **"Instructions for Use"** at the end of this leaflet.
- The injection site should be alternated. New injections should be given at least 3 cm away from a previous injection site. No injection should be given into areas where the skin is within 5 cm of your belly button (navel), or is tender, damaged, bruised, or scarred. If other medicines for subcutaneous injection are used during the treatment course with Remsima, a different injection site should be used.
- Remsima should not be mixed or diluted with other products.

If you use more Remsima than you should
If you have used more Remsima than you should (either by injecting too much on a single occasion or by using it too frequently), talk to a doctor, pharmacist or nurse immediately. Always have the outer carton of the medicine with you, even if it is empty.

If you forget to use Remsima
If you miss a dose of Remsima, you should skip the missed dose and take your next dose at your regular scheduled date. Do not take a double dose on the same day to make up for a forgotten dose. If you are not sure when to inject Remsima, call your doctor.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets 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 your treatment with Remsima has stopped.

Tell your doctor straight away if you notice any of the following:
- **Signs of an allergic reaction** such as swelling of your face, lips, mouth or throat which may cause difficulty in swallowing or breathing, skin rash, hives, swelling of the hands, feet or ankles. An allergic reaction could happen within 2 hours of your injection or later. Other 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 heart problem** such as chest discomfort or pain, arm pain, stomach pain, shortness of breath, anxiety, lightheadedness, dizziness, fainting, sweating, nausea (feeling sick), vomiting, fluttering or pounding in your chest, a fast or a slow heartbeat, and swelling of your feet
- **Signs of infection (including TB)** such as fever, feeling tired, cough which may be persistent, shortness of breath, flu-like symptoms, weight loss, night sweats, diarrhoea, wounds, dental problems or burning sensation when urinating
- **Signs of a lung problem** such as coughing, breathing difficulties or tightness in the chest
- **Signs of a nervous system problem (including eye problems)** such as fits, tingling or numbness in any part of your body, weakness in arms or legs, changes in eyesight such as double vision or other eye problems
- **Signs of a liver problem** such as yellowing of the skin or eyes, dark-brown coloured urine or pain in the upper right side of the stomach area, 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
- **Signs of a low blood count** such as persistent fever, bleeding or bruising more easily or looking pale.

Tell your doctor straight away if you notice any of the above.

The known other side effects of Remsima include the following in groups of deceasing frequency:

Very common (may affect more than 1 in 10 people)

- Stomach pain, feeling sick
- Viral infections such as herpes or flu
- Upper respiratory infections such as sinusitis
- Headache
- Side effect due to an injection
- Pain.

Common (may affect up to 1 in 10 people)
- Changes in how your liver works, increase in liver enzymes (shown in blood tests)
- Lung or chest infections such as bronchitis or pneumonia
- Fungal infection of the skin
- Difficult or painful breathing, chest pain
- Bleeding in the stomach or intestines, diarrhoea, indigestion, heartburn, constipation
- Nettle-type rash (hives), itchy rash or dry skin
- Balance problems or feeling dizzy
- Fever, increased sweating
- Circulation problems such as low or high blood pressure
- Bruising, hot flush or nosebleed, warm, red skin (flushing)
- Feeling tired or weak
- Bacterial infections such as blood poisoning, abscess or infection of the skin (cellulitis)
- Blood problems such as anaemia or low white blood cell count
- Swollen lymph nodes
- Depression, problems sleeping
- 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 or itching
- Chills, a build-up of fluid under the skin causing swelling
- Feeling numb or having a tingling feeling.

Uncommon (may affect up to 1 in 100 people)
- Tuberculosis
- Shortage of blood supply, swelling of a vein
- Skin problems such as blistering, warts, abnormal skin colouration or pigmentation, or swollen lips
- Severe allergic reactions (e.g. anaphylaxis), an immune system disorder called lupus, allergic reactions to foreign proteins
- Wounds taking longer to heal
- Thickening of the skin, nail
- 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 sties, infection of cornea (clear window of the eye)
- New or worsening heart failure, slow heart rate
- Fainting
- Convulsions, nerve problems
- A hole in the bowel or blockage of the intestine, stomach pain or cramps
- Swelling of your pancreas (pancreatitis)
- Fungal infections such as yeast infection, including fungal infection of the toenails or fingernails
- Lung problems (such as oedema)
- Fluid around the lungs (pleural effusion), inflammation of layers covering the lungs (pleurisy)

- Kidney infections
- Low platelet count, too many white blood cells, bruise or black and blue mark
- Infections of the vagina
- Positive antibodies that are formed
- Sleepiness.

Rare (may affect up to 1 in 1,000 people)
- A type of blood cancer (lymphoma)
- Your blood not supplying enough oxygen to your body, circulation problems such as narrowing of a blood vessel
- Inflammation of the lining of the brain (meningitis)
- Infections due to a weakened immune system
- Hepatitis B infection when you have had hepatitis B in the past
- Inflammation of liver due to immune system attacking the liver
- Small area of inflammation in tissue
- Abnormal tissue swelling or growth
- Swelling of small blood vessels (vasculitis)
- Immune disorders that could affect the lungs, skin and lymph nodes (such as sarcoidosis)
- Lack of interest or emotion
- Serious skin problems such as toxic epidermal necrolysis, Stevens-Johnson Syndrome or erythema multiforme, skin problems such as boils
- Serious nervous system disorders such as transverse myelitis, multiple sclerosis-like disease, optic neuritis and Guillain-Barré syndrome
- 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 counts, including a severely decreased number of white blood cells.
- Jaundice (skin and eyes turning yellow)
- Severe allergic reactions causing loss of consciousness (anaphylactic shock)
- Inflammation of the interior of the eye
- Low or absent protein that help fight infection and blood clotting
- A blood disorder that causes blood clots to form in small blood vessels. This leads to a low platelet count
- Deficiency of all three cellular components of the blood (red cells, white cells, and platelets)
- A condition in which red blood cells are destroyed and removed from the bloodstream before their normal lifespan is over
- A bleeding disorder in which the immune system destroys platelets, which are necessary for normal blood clotting
- Small red or purple spots caused by bleeding into the skin
- Bluish discoloration of the skin resulting from poor circulation or inadequate oxygenation of the blood
- A marked decrease in the number of granulocytes (a type of white blood cell) in newborn children after in utero exposure to infliximab.

Not known (frequency cannot be estimated from the available data)
- Cancer in children and adults
- A rare blood cancer affecting mostly young males (hepatosplenic T-cell lymphoma)
- Liver failure
- Merkel cell carcinoma (a type of skin cancer)
- Worsening of a condition called dermatomyositis (seen as a skin rash accompanying muscle weakness)
- Temporary loss of sight during or within 2 hours of injection
- Infection due to weakened immune system following use of live vaccines

- Heart attack
- Vaccine related infection in newborn children (after in utero exposure to infliximab).

5. How to store Remsima

The storage details should you need them are as follows:

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the label and the carton after "EXP". The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C - 8°C). Do not freeze. Keep the medicinal product in its outer carton to protect from light.
- 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 14 days, but not beyond the original expiry date. In this situation, do not return to refrigerated storage again. Write the new expiry date on the carton including day/month/year. Discard this medicine if not used by the new expiry date or the expiry date printed on the carton, whichever is earlier.
- Do not use this medicine if you notice that the liquid is different to clear colourless or pale brown or see any particles present.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Remsima contains
- The active substance is infliximab. Each pre-filled syringe with passive safety guard contains 120 mg/mL of infliximab.
- The other ingredients are acetic acid, sodium acetate trihydrate, sorbitol, polysorbate 80 and water for injection.

What Remsima looks like and contents of the pack
Remsima is clear to opalescent, colourless to pale brown solution which is supplied as a single use pre-filled syringe with passive safety guard.

Remsima is produced in packs of 1, 2 or 4 pre-filled syringes with passive safety guard. Not all pack sizes may be marketed.

Product License Holder
CELLTRION HEALTHCARE SINGAPORE
PRIVATE LIMITED
8 CROSS STREET
#10-00 PWC BUILDING
SINGAPORE (048424)

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7. Instructions for use

Remsima (established name)

Single-Use Pre-Filled Syringe with Passive Safety Guard for Subcutaneous Injection
120 mg/1.0 mL

Read carefully these instructions before using the Remsima Syringe. Consult your healthcare provider if you have questions about using the Remsima Syringe.

Important information

- Use the Syringe **ONLY if** your healthcare provider has trained you on the right way to prepare for and to give an injection.
- Ask your healthcare provider how often you will need to give an injection.
- Rotate the injection site each time you give an injection. Each new injection site should be at least 3 cm away from the previous injection site.

⚠ **Warning! Do not use** the Syringe if it has been dropped or is visibly damaged.
⚠ **Warning! Do not** reuse the Syringe.
⚠ **Warning! Do not** shake the Syringe at any time.

About the Remsima Syringe

Parts of the Syringe (see *Figure A*):

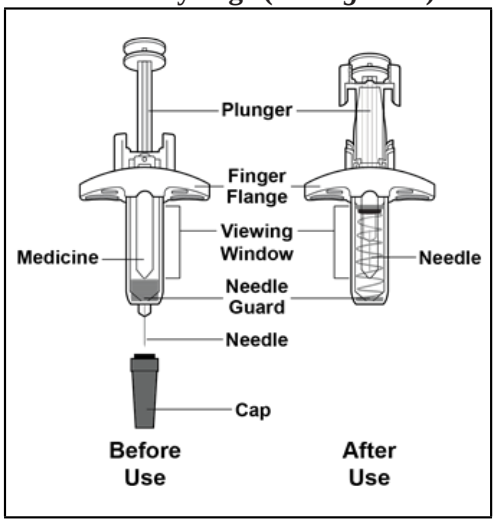

Figure A

⚠ **Caution! Do not** remove the Cap until you are ready to inject. Once you remove the Cap, do not recap the Syringe.

How to store the Syringe

- Store the Syringe in a refrigerator at 2°C to 8ºC.
- Keep the Syringe in the original carton to protect it from light.

⚠ **Warning! Do not freeze** the Syringe. If the Syringe has been frozen, do not use the Syringe even if it is thawed.
⚠ **Warning! Do not** warm the Syringe using heat sources such as hot water or a microwave. Let the Syringe naturally warm at room temperature for 30 minutes before giving an injection.

- You may store the Syringe at room temperature between 20°C to 25°C for up to 14 days.
- Once the Syringe has reached room temperature, **do not** put it back in the refrigerator.

- Keep the Syringe and injection supplies out of the sight and reach of children.

Prepare for the injection

1. Gather the supplies for the injection.

a. Prepare a clean, flat surface, such as a table or countertop, in a well-lit area.
b. Remove the Syringe from the carton by holding the middle of the Syringe Body.
c. Ensure you have the following supplies:
- Syringe
- Alcohol swab
- Cotton ball or gauze*
- Adhesive bandage*
- Sharps disposal container*

**Items not included in the carton.*

2. Inspect the Syringe.

a. Look at the Syringe and confirm that it does not show signs of damage and that the expiration date has not passed (see *Figure B*).

⚠ **Warning! Do not** use the Syringe if:
- It is cracked or damaged.
- The expiration date has passed.

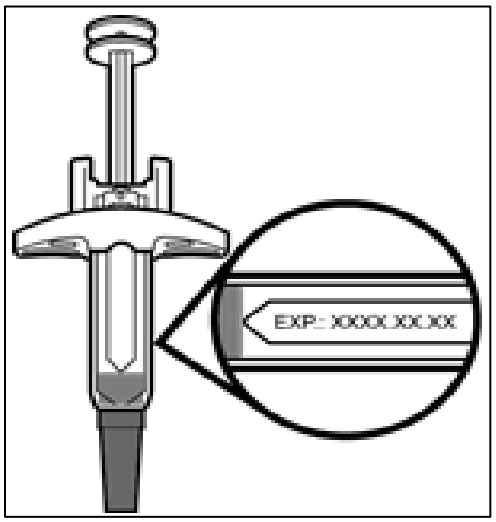

Figure B

3. Inspect the Medicine.

a. Look through the Viewing Window and confirm that the liquid is clear and colourless or pale brown (see *Figure C*).

⚠ **Warning! Do not** use the Syringe if the liquid is different to clear colourless or pale brown or contains particles in it.

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

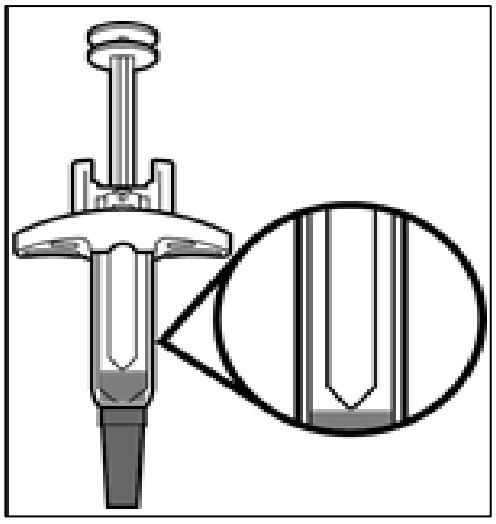

Figure C

4. Wait 30 minutes.

a. Leave the Syringe at room temperature for 30 minutes to allow it to naturally warm up (see *Figure D*).

⚠ **Warning! Do not** warm the Syringe using heat sources such as hot water or a microwave.

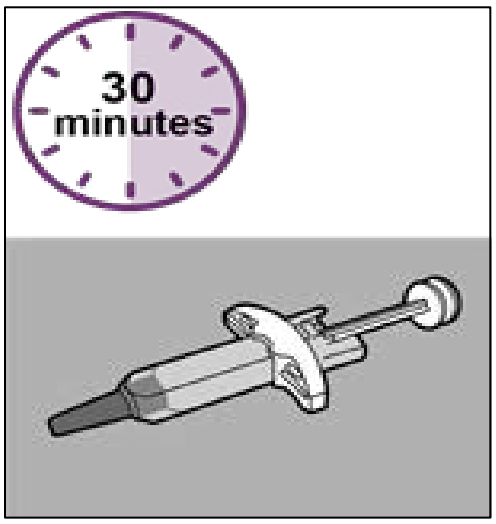

Figure D

5. Choose an injection site (see *Figure E*).

a. Select an injection site. You may inject into:

- The front of the thighs.
- The abdomen except for the 5 cm around the belly button (navel).
- The outer area of the upper arms (caregiver ONLY).

⚠ **Warning! Do not** inject into skin that is within 5 cm of your belly button (navel), or is tender, damaged, bruised, or scarred.

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

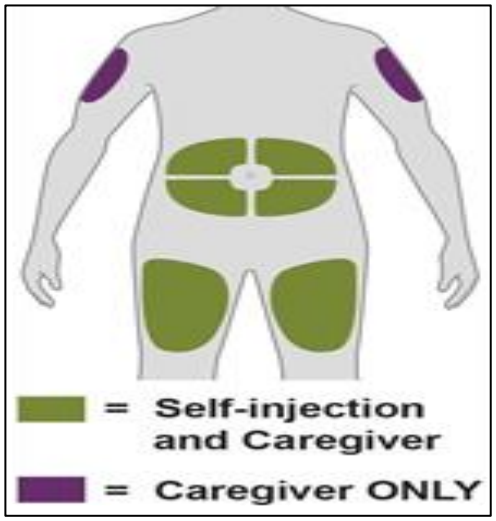

Figure E

6. Wash your hands.

a. Wash your hands with soap and water and dry them thoroughly (see *Figure F*).

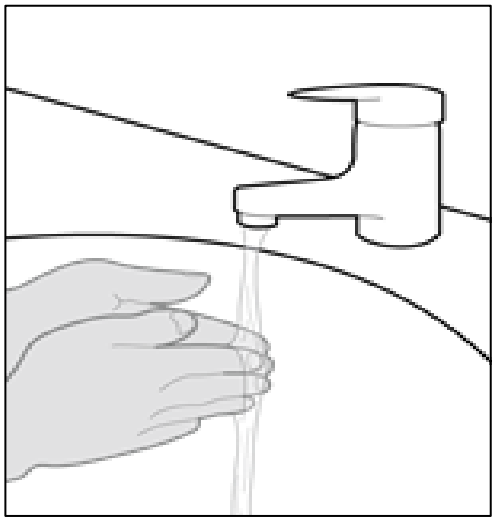

Figure F

7. Clean the injection site.

a. Clean the injection site with an alcohol swab (see *Figure G*).
b. Let the skin dry before injecting.

⚠ **Warning! Do not** blow on or touch the injection site again before giving the injection.

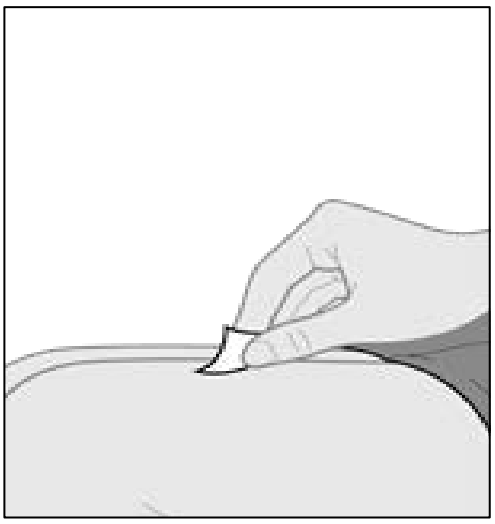

Figure G

Give the injection

8. Remove the Cap.

a. Pull the Cap straight off and set it aside (see *Figure H*).

⚠ **Warning! Do not** remove the Cap until you are ready to inject.

⚠ **Warning! Do not** try to put the needle cover back onto the Syringe.

⚠ **Warning! Do not** touch the Needle. Doing so may result in a needle stick injury.

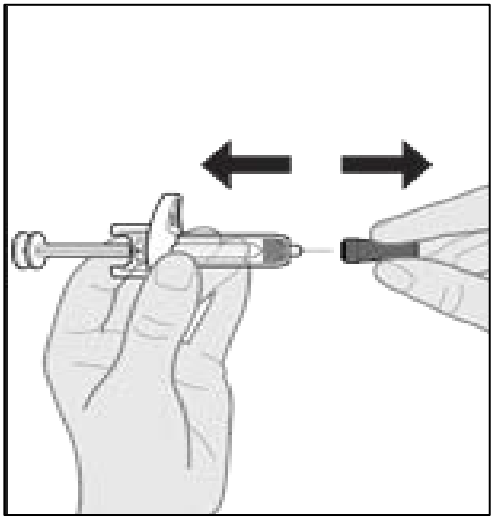

Figure H

9. Insert the Syringe into the injection site.

a. Gently pinch a fold of skin at the injection site with one hand.
b. With a quick and "dart-like" motion, insert the Needle completely into the fold of the skin at a 45-degree angle (see *Figure I*).

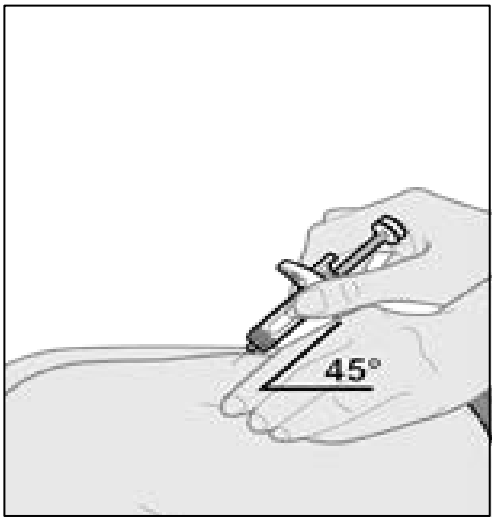

Figure I

10. Give the injection.

a. After the Needle is inserted, release the pinch.
b. Push the Plunger down slowly and as far as it will go until the Syringe is empty (see *Figure J*).

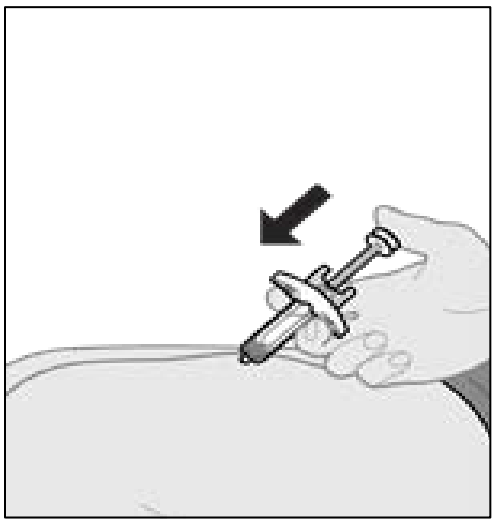

Figure J

11. Remove the Syringe from the injection site.

a. After the Syringe is empty, slowly lift your thumb from the Plunger until Needle is completely covered by the Needle Guard (see *Figure K*).

⚠ **Warning! Do not** re-use the Syringe.
⚠ **Warning! Do not** touch the Needle.

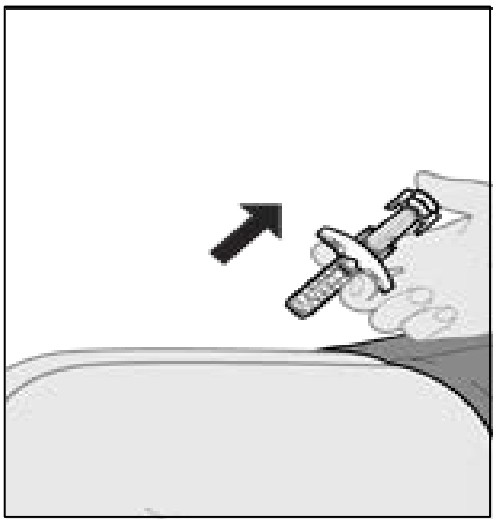

Figure K

After the injection

12. Dispose of the Syringe.

a. Put the used Syringe and Cap in an approved sharps disposal container immediately after use (see *Figure L*).

⚠ **Warning! Do not** throw away (dispose of) the Syringes in your household waste.

If you do not have an approved sharps disposal container, you may use a household container that is:

- made of a heavy-duty plastic;
- able to close with a tight-fitting, puncture-resistant lid, without sharps being able to come out;
- upright and stable during use;
- leak-resistant; and
- properly labelled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, it

Figure L

should be disposed of in accordance with local requirements.

13. Care for the injection site.

a. Treat the injection site by gently pressing a cotton ball or gauze to the site and apply an adhesive bandage, if necessary.

Package leaflet: Information for the user

Remsima 120 mg solution for injection in pre-filled pen
Infliximab

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- Your doctor will also give you a Patient Alert Card, which contains important safety information you need to be aware of before and during your treatment with Remsima.
- When starting a new card, keep this card as a reference for 4 months after your last dose of Remsima.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Remsima is and what it is used for

Remsima 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 (tumour necrosis factor) alpha.

Remsima belongs to a group of medicines called 'TNF blockers'. It is used in adults for the following inflammatory diseases:
- Rheumatoid arthritis
- Psoriatic arthritis
- Ankylosing spondylitis (Bechterew's disease)
- Psoriasis.

Remsima works by selectively attaching to TNF alpha and blocking its action. TNF alpha is involved in inflammatory processes of the body so blocking it can reduce the inflammation in your body.

Rheumatoid arthritis
Rheumatoid arthritis is an inflammatory disease of the joints. If you have active rheumatoid arthritis you will first be given other medicines. If these medicines do not work well enough, you will be given Remsima which you will take with another medicine called methotrexate to:
- reduce the signs and symptoms of your disease,
- slow down the damage in your joints,
- improve your physical function.

Psoriatic arthritis

Psoriatic arthritis is an inflammatory disease of the joints, usually accompanied by psoriasis. If you have active psoriatic arthritis you will first be given other medicines. If these medicines do not work well enough, you will be given Remsima to:
- reduce the signs and symptoms of your disease,
- slow down the damage in your joints,
- improve your physical function.

Ankylosing spondylitis (Bechterew's disease)
Ankylosing spondylitis is an inflammatory disease of the spine. If you have ankylosing spondylitis you will first be given other medicines. If these medicines do not work well enough, you will be given Remsima to:
- reduce the signs and symptoms of your disease,
- improve your physical function.

Psoriasis
Psoriasis is an inflammatory disease of the skin. If you have moderate to severe plaque psoriasis, you will first be given other medicines or treatments, such as phototherapy. If these medicines or treatments do not work well enough, you will be given Remsima to reduce the signs and symptoms of your disease.

2. What you need to know before you use Remsima

You must not use Remsima if
- you are allergic to infliximab or any of the other ingredients of this medicine (listed in section 6),
- you are allergic to proteins that come from mice,
- you have tuberculosis (TB) or another serious infection such as pneumonia or sepsis (serious bacterial infection of the blood),
- you have heart failure that is moderate or severe.

Do not use Remsima if any of the above applies to you. If you are not sure, talk to your doctor before you are given Remsima.

Warnings and precautions
Talk to your doctor before using Remsima, if you have:

<u>Had treatment with any medicine containing infliximab before</u>

- Tell your doctor if you have had treatment with medicines containing infliximab in the past and are now starting Remsima treatment again.
- If you have had a break in your treatment with infliximab of more than 16 weeks, there is a higher risk for allergic reactions when you start the treatment again.

<u>Allergic reactions</u>

- Some patients receiving infliximab have experienced allergic reactions. Some of these reactions were severe and potentially life-threatening. These reactions can happen while you are getting your Remsima treatment or shortly afterward. Signs of an allergic reaction can include hives (red, raised, itchy patches of skin), high or low blood pressure, difficulty breathing, fever, chest pain, chills or loss of consciousness.
- Tell your doctor straightaway if you experience any of these signs during or within a few hours following your treatment.
- Your doctor may need to stop or pause your treatment and may give you medicines to treat the allergic reaction. Also, for your next injection, your doctor may give you medications such as antihistamine or paracetamol before the injection.

- Also, some patients treated with infliximab have had delayed allergic reactions. The delayed reactions occurred 3 to 12 days after receiving treatment with infliximab. Tell your doctor right away if you have any of these signs of delayed allergic reaction to Remsima including fever, muscle or joint pain, rash, swelling of the face and hands, headache, difficulty swallowing or sore throat.

Infections

- Tell your doctor before you are given Remsima if you have an infection even if it is a very minor one.
- Tell your doctor before you are given Remsima if you have ever lived in or travelled to an area where infections called histoplasmosis, coccidioidomycosis, or blastomycosis are common. These infections are caused by specific types of fungi that can affect the lungs or other parts of your body.
- You may get infections more easily when you are being treated with Remsima. If you are 65 years of age or older, you have a greater 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 straight away if you get signs of infection during treatment with Remsima. Signs include fever, cough, flu-like signs, feeling unwell, red or hot skin, wounds or dental problems. Your doctor may recommend temporarily stopping Remsima.

Tuberculosis (TB)

- It is very important that you tell your doctor if you have ever had TB or if you have been in close contact with someone who has had or has TB.
- Your doctor 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 doctor will record these tests on your Patient Alert Card.
- If your doctor feels that you are at risk for TB, you may be treated with medicines for TB before you are given Remsima.

Tell your doctor straight away if you get signs of TB during treatment with Remsima. Signs include persistent cough, weight loss, feeling tired, fever, night sweats.

Hepatitis B virus

- Tell your doctor before you are using Remsima 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 hepatitis B.
- Your doctor should test you for hepatitis B virus.
- Treatment with TNF blockers such as Remsima 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 and may give you medicines such as effective antiviral therapy with supportive treatment.

Liver problems

- Some patients receiving infliximab have developed serious liver problems.
- Tell your doctor if you experience jaundice (skin and eyes turning yellow), dark brown-coloured urine, extreme tiredness (severe fatigue) or pain on the right side of your stomach area (right-sided abdominal pain).

Lupus-like problems

- Some patients have developed symptoms that are like the symptoms of Lupus.

- If you develop any of the following symptoms, your doctor may decide to stop your treatment with Remsima: chest discomfort or pain that does not go away, joint pain, shortness of breath, rash on the cheeks or arms that gets worse in the sun.

Heart problems

- Tell your doctor if you have any heart problems, such as mild heart failure.
- Your doctor will want to closely monitor your heart.

Tell your doctor straight away if you get new or worsening signs of heart failure during treatment with Remsima. Signs include shortness of breath or swelling of your feet.

Blood problems

- 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 doctor if you have a fever that does not go away, look very pale, bruise or bleed very easily.
- Your doctor may stop Remsima if your blood disorder is significant.

Cancer and lymphoma

- Tell your doctor before you are given Remsima if you have or have ever had lymphoma (a type of blood cancer) or any other cancer.
- Patients with severe rheumatoid arthritis, who have had the disease for a long time, may be at higher risk of developing lymphoma.
- Adults taking Remsima may have an increased risk of developing lymphoma or another 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 has usually resulted in death. Almost all patients had also received medicines containing azathioprine or 6-mercaptopurine in addition to TNF-blockers.
- Some patients treated with infliximab have developed certain kinds of skin cancer. If there are any changes in your skin or growths on the skin during or after therapy, tell your doctor.
- Some women being treated for rheumatoid arthritis with infliximab have developed cervical cancer. For women taking Remsima including those over 60 years of age, your doctor may recommend regular screening for cervical cancer.

Lung disease or heavy smoking

- Tell your doctor before you are given Remsima 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 have a higher risk of developing cancer with Remsima treatment.

Nervous system disease

- Tell your doctor before you are given Remsima if you have or have ever had a problem that affects your nervous system. This includes multiple sclerosis, Guillain-Barré syndrome, if you have fits or have been diagnosed with 'optic neuritis'.

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

Abnormal skin openings

- Tell your doctor if you have any abnormal skin openings (fistulae) before you are given Remsima.

Vaccinations

- Talk to your doctor if you recently have had or are due to have a vaccine.
- You should receive recommended vaccinations before starting Remsima treatment. You may receive some vaccines during treatment with Remsima but you should not receive live vaccines (vaccines that contain a living but weakened infectious agent) while using Remsima because they may cause infections.
- If you received Remsima while you were pregnant, your baby may also be at higher risk for getting an infection with live vaccines for up to six months after birth. It is important that you tell your baby's doctors and other health care professionals about your Remsima use so they can decide when your baby should receive any vaccine, including live vaccines such as BCG (used to prevent tuberculosis). For more information see section on Pregnancy and breast-feeding.

Therapeutic infectious agents

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

Operations or dental procedures

- Tell your doctor if you are going to have any operations or dental procedures.
- Tell your surgeon or dentist that you are having treatment with Remsima by showing them your Patient Alert Card.

Children and adolescents
Remsima is not recommended for subcutaneous administration to children and adolescents under 18 years old. This is because there is no experience of using the medicine in these age groups.

Other medicines and Remsima
Patients who have inflammatory diseases already take medicines to treat their problem. These medicines may cause side effects. Your doctor will advise you what other medicines you must keep using while you are having Remsima.

Tell your doctor if you are using, have recently used or might use any other medicines, including any other medicines to treat 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 your immune system.
- Kineret (which contains anakinra). Remsima and Kineret should not be used together.
- Orencia (which contains abatacept). Remsima and Orencia should not be used together.

While using Remsima you should not receive live vaccines. If you were using Remsima during pregnancy, tell your baby’s doctor and other health care professionals caring for your baby about your Remsima use before the baby receives any vaccines.

If you are not sure if any of the above applies to you, talk to your doctor, pharmacist or nurse before using Remsima.

Pregnancy, breast-feeding and fertility
- If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. Remsima should only be used during pregnancy if your doctor feels it is necessary for you.

- You should avoid getting pregnant when you are being treated with Remsima and for 6 months after you stop being treated with it. Discuss the use of contraception during this time with your doctor.
- Do not breast-feed when you are being treated with Remsima or for 6 months after your last treatment with Remsima.
- If you received Remsima during your pregnancy, your baby may have a higher risk for getting an infection.
- It is important that you tell your baby's doctors and other healthcare professionals about your Remsima use before your baby is given any vaccine. If you received Remsima 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 section on vaccination.
- 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 fevers or infections, contact your baby's doctor immediately.

Driving and using machines
Remsima is not likely to affect your ability to drive or use tools or machines. If you feel tired, dizzy, or unwell after having Remsima, do not drive or use any tools or machines.

Remsima contains Sorbitol
Sorbitol is a source of fructose. If your doctor has told you that you have an intolerance to some sugars or if you have been diagnosed with hereditary fructose intolerance (HFI), a rare genetic disorder in which a person cannot break down fructose, talk to your doctor before you take or receive this medicine.

3. How to use Remsima

Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

Rheumatoid arthritis
Your doctor will start your treatment with two Remsima doses of 3 mg for every kg of body weight administered 2 weeks apart via intravenous infusion (given to you into a vein, usually in your arm, over a period of 2 hours). The first subcutaneous injection (injection under the skin) of Remsima will be given after 4 weeks from the last intravenous infusion. The usual recommended dose of Remsima administered subcutaneously is 120 mg once every 2 weeks regardless of weight.

Psoriatic arthritis, ankylosing spondylitis (Bechterew's disease) and psoriasis
Your doctor will start your treatment with two Remsima doses of 5 mg for every kg of body weight administered 2 weeks apart via intravenous infusion (given to you into a vein, usually in your arm, over a period of 2 hours). The first subcutaneous injection (injection under the skin) of Remsima will be given after 4 weeks from the last intravenous infusion. The usual recommended dose of Remsima administered subcutaneously is 120 mg once every 2 weeks if your body weight is below 80 kg or 240 mg (two injections of Remsima 120 mg) once every 2 weeks if your body weight is at or above 80 kg.

How Remsima is given
- It is important to check the product labels to ensure that the correct formulation is being given as prescribed. Remsima 120 mg is designed only for subcutaneous administration and is not for intravenous use.
- The first two Remsima intravenous infusions will be given to you by your doctor or nurse.
- At the two Remsima treatment via intravenous infusions, your doctor or nurse may inject Remsima subcutaneously. However, you and your doctor may decide that you can inject Remsima yourself. In this case, you will get training on how to inject Remsima yourself.

- Talk to your doctor if you have any questions about giving yourself an injection. You will find detailed **"Instructions for Use"** at the end of this leaflet.
- The injection site should be alternated. New injections should be given at least 3 cm away from a previous injection site. No injection should be given into areas where the skin is within 5 cm of your belly button (navel), or is tender, damaged, bruised, or scarred. If other medicines for subcutaneous injection are used during the treatment course with Remsima, a different injection site should be used.
- Remsima should not be mixed or diluted with other products.

If you use more Remsima than you should
If you have used more Remsima than you should (either by injecting too much on a single occasion or by using it too frequently), talk to a doctor, pharmacist or nurse immediately. Always have the outer carton of the medicine with you, even if it is empty.

If you forget to use Remsima
If you miss a dose of Remsima, you should skip the missed dose and take your next dose at your regular scheduled date. Do not take a double dose on the same day to make up for a forgotten dose. If you are not sure when to inject Remsima, call your doctor.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets 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 your treatment with Remsima has stopped.

Tell your doctor straight away if you notice any of the following:
- **Signs of an allergic reaction** such as swelling of your face, lips, mouth or throat which may cause difficulty in swallowing or breathing, skin rash, hives, swelling of the hands, feet or ankles. An allergic reaction could happen within 2 hours of your injection or later. Other 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 heart problem** such as chest discomfort or pain, arm pain, stomach pain, shortness of breath, anxiety, lightheadedness, dizziness, fainting, sweating, nausea (feeling sick), vomiting, fluttering or pounding in your chest, a fast or a slow heartbeat, and swelling of your feet
- **Signs of infection (including TB)** such as fever, feeling tired, cough which may be persistent, shortness of breath, flu-like symptoms, weight loss, night sweats, diarrhoea, wounds, dental problems or burning sensation when urinating
- **Signs of a lung problem** such as coughing, breathing difficulties or tightness in the chest
- **Signs of a nervous system problem (including eye problems)** such as fits, tingling or numbness in any part of your body, weakness in arms or legs, changes in eyesight such as double vision or other eye problems
- **Signs of a liver problem** such as yellowing of the skin or eyes, dark-brown coloured urine or pain in the upper right side of the stomach area, 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
- **Signs of a low blood count** such as persistent fever, bleeding or bruising more easily or looking pale.

Tell your doctor straight away if you notice any of the above.

The known other side effects of Remsima include the following in groups of deceasing frequency:

Very common (may affect more than 1 in 10 people)

- Stomach pain, feeling sick
- Viral infections such as herpes or flu
- Upper respiratory infections such as sinusitis
- Headache
- Side effect due to an injection
- Pain.

Common (may affect up to 1 in 10 people)
- Changes in how your liver works, increase in liver enzymes (shown in blood tests)
- Lung or chest infections such as bronchitis or pneumonia
- Fungal infection of the skin
- Difficult or painful breathing, chest pain
- Bleeding in the stomach or intestines, diarrhoea, indigestion, heartburn, constipation
- Nettle-type rash (hives), itchy rash or dry skin
- Balance problems or feeling dizzy
- Fever, increased sweating
- Circulation problems such as low or high blood pressure
- Bruising, hot flush or nosebleed, warm, red skin (flushing)
- Feeling tired or weak
- Bacterial infections such as blood poisoning, abscess or infection of the skin (cellulitis)
- Blood problems such as anaemia or low white blood cell count
- Swollen lymph nodes
- Depression, problems sleeping
- 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 or itching
- Chills, a build-up of fluid under the skin causing swelling
- Feeling numb or having a tingling feeling.

Uncommon (may affect up to 1 in 100 people)
- Tuberculosis
- Shortage of blood supply, swelling of a vein
- Skin problems such as blistering, warts, abnormal skin colouration or pigmentation, or swollen lips
- Severe allergic reactions (e.g. anaphylaxis), an immune system disorder called lupus, allergic reactions to foreign proteins
- Wounds taking longer to heal
- Thickening of the skin, nail
- 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 sties, infection of cornea (clear window of the eye)
- New or worsening heart failure, slow heart rate
- Fainting
- Convulsions, nerve problems
- A hole in the bowel or blockage of the intestine, stomach pain or cramps
- Swelling of your pancreas (pancreatitis)
- Fungal infections such as yeast infection, including fungal infection of the toenails or fingernails
- Lung problems (such as oedema)
- Fluid around the lungs (pleural effusion), inflammation of layers covering the lungs (pleurisy)

- Kidney infections
- Low platelet count, too many white blood cells, bruise or black and blue mark
- Infections of the vagina
- Positive antibodies that are formed
- Sleepiness.

Rare (may affect up to 1 in 1,000 people)
- A type of blood cancer (lymphoma)
- Your blood not supplying enough oxygen to your body, circulation problems such as narrowing of a blood vessel
- Inflammation of the lining of the brain (meningitis)
- Infections due to a weakened immune system
- Hepatitis B infection when you have had hepatitis B in the past
- Inflammation of liver due to immune system attacking the liver
- Small area of inflammation in tissue
- Abnormal tissue swelling or growth
- Swelling of small blood vessels (vasculitis)
- Immune disorders that could affect the lungs, skin and lymph nodes (such as sarcoidosis)
- Lack of interest or emotion
- Serious skin problems such as toxic epidermal necrolysis, Stevens-Johnson Syndrome or erythema multiforme, skin problems such as boils
- Serious nervous system disorders such as transverse myelitis, multiple sclerosis-like disease, optic neuritis and Guillain-Barré syndrome
- 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 counts, including a severely decreased number of white blood cells.
- Jaundice (skin and eyes turning yellow)
- Severe allergic reactions causing loss of consciousness (anaphylactic shock)
- Inflammation of the interior of the eye
- Low or absent protein that help fight infection and blood clotting
- A blood disorder that causes blood clots to form in small blood vessels. This leads to a low platelet count
- Deficiency of all three cellular components of the blood (red cells, white cells, and platelets)
- A condition in which red blood cells are destroyed and removed from the bloodstream before their normal lifespan is over
- A bleeding disorder in which the immune system destroys platelets, which are necessary for normal blood clotting
- Small red or purple spots caused by bleeding into the skin
- Bluish discoloration of the skin resulting from poor circulation or inadequate oxygenation of the blood
- A marked decrease in the number of granulocytes (a type of white blood cell) in newborn children after in utero exposure to infliximab.

Not known (frequency cannot be estimated from the available data)
- Cancer in children and adults
- A rare blood cancer affecting mostly young males (hepatosplenic T-cell lymphoma)
- Liver failure
- Merkel cell carcinoma (a type of skin cancer)
- Worsening of a condition called dermatomyositis (seen as a skin rash accompanying muscle weakness)
- Temporary loss of sight during or within 2 hours of injection
- Infection due to weakened immune system following use of live vaccines

- Heart attack
- Vaccine related infection in newborn children (after in utero exposure to infliximab).

5. How to store Remsima

The storage details should you need them are as follows:

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the label and the carton after "EXP". The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C - 8°C). Do not freeze. Keep the medicinal product in its outer carton to protect from light.
- 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 14 days, but not beyond the original expiry date. In this situation, do not return to refrigerated storage again. Write the new expiry date on the carton including day/month/year. Discard this medicine if not used by the new expiry date or the expiry date printed on the carton, whichever is earlier.
- Do not use this medicine if you notice that the liquid is different to clear colourless or pale brown or see any particles present.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Remsima contains
- The active substance is infliximab. Each pre-filled pen contains 120 mg/mL of infliximab.
- The other ingredients are acetic acid, sodium acetate trihydrate, sorbitol, polysorbate 80 and water for injection.

What Remsima looks like and contents of the pack
Remsima is clear to opalescent, colourless to pale brown solution which is supplied as a single use pre-filled pen.

Remsima is produced in packs of 1, 2 or 4 pre-filled pens with passive safety guard. Not all pack sizes may be marketed.

Product License Holder
CELLTRION HEALTHCARE SINGAPORE
PRIVATE LIMITED
8 CROSS STREET
#10-00 PWC BUILDING
SINGAPORE (048424)

This leaflet was last revised in {02/2019}

7. Instructions for use

Remsima (established name)

Single-Use Pre-Filled Pen for Subcutaneous Injection
120 mg/1.0 mL

Read carefully these instructions before using the Remsima Pen. Consult your healthcare provider if you have questions about using the Remsima Pen.

Important information

- Use the Pen **ONLY if** your healthcare provider has trained you on the right way to prepare for and to give an injection.
- Ask your healthcare provider how often you will need to give an injection.
- Rotate the injection site each time you give an injection. Each new injection site should be at least 3 cm away from the previous injection site.

⚠ **Warning! Do not** use the Pen if it has been dropped or is visibly damaged.
⚠ **Warning! Do not** reuse the Pen.
⚠ **Warning! Do not** shake the Pen at any time.

About the Remsima Pen

Parts of the Pen (see *Figure A*):

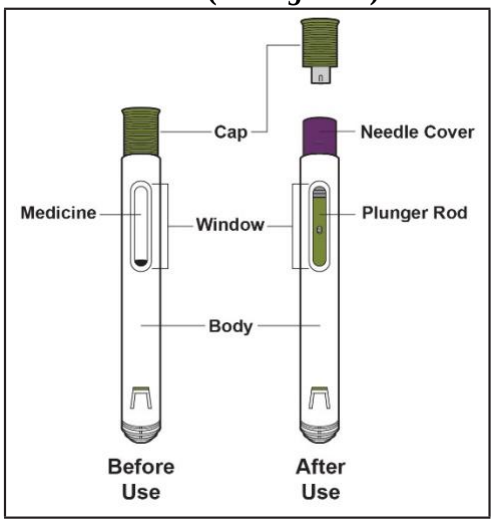

Figure A

⚠ **Caution! Do not** remove the Cap until you are ready to inject. Once you remove the Cap, **do not** recap the Pen.

How to store the Pen

- Store the Pen in a refrigerator at 2°C to 8ºC.
- Keep the Pen in the original carton to protect it from light.

⚠ **Warning! Do not** freeze the Pen. If the Pen has been frozen, **do not** use the Pen even if it is thawed.

⚠ **Warning! Do not** warm the Pen using heat sources such as hot water or a microwave. Let the Pen naturally warm at room temperature for 30 minutes before giving an injection.

- You may store the Pen at room temperature between 20°C to 25°C for up to 14 days.
- Once the Pen has reached room temperature, **do not** put it back in the refrigerator.
- Keep the Pen and injection supplies out of the sight and reach of children.

Prepare for the injection

1. Gather the supplies for the injection.

a. Prepare a clean, flat surface, such as a table or countertop, in a well-lit area.
b. Remove the Pen from the carton stored in your refrigerator.
c. Ensure you have the following supplies:

- Pen
- Alcohol swab
- Cotton ball or gauze*
- Adhesive bandage*
- Sharps disposal container*

**Items not included in the carton.*

2. Inspect the Pen.

a. Look at the Pen and confirm that it does not show signs of damage and that the expiration date has not passed (see *Figure B*).

⚠ **Warning! Do not** use the Pen if:

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

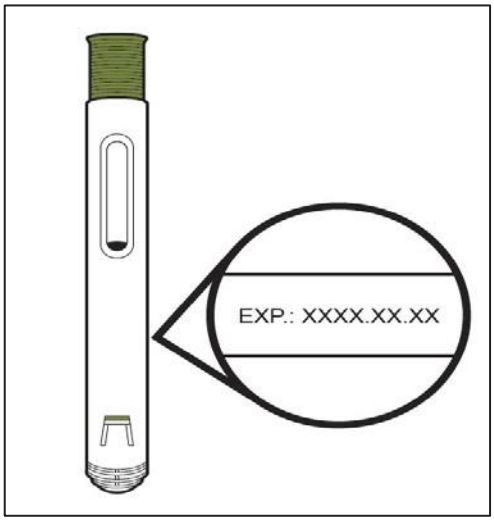

Figure B

3. Inspect the Medicine.

a. Look through the Window and confirm that the liquid is clear and colourless or pale brown (see *Figure C*).

⚠ **Warning! Do not** use the Pen if the liquid is different to clear colourless or pale brown or contains particles in it.

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

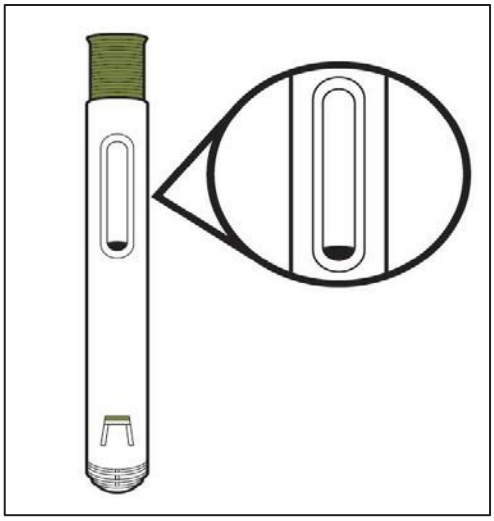

Figure C

4. Wait 30 minutes.

a. Leave the Pen at room temperature for 30 minutes to allow it to naturally warm up (see *Figure D*).

⚠ **Warning! Do not** warm the Pen using heat sources such as hot water or a microwave.

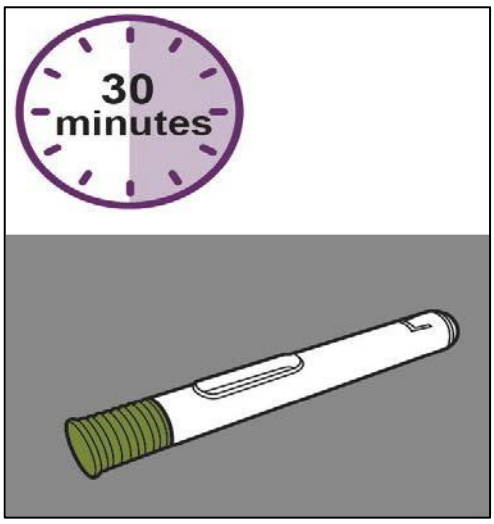

Figure D

5. Choose an injection site (see *Figure E*).

a. Select an injection site. You may inject into:

- The front of the thighs.
- The abdomen except for the 5 cm around the belly button (navel).
- The outer area of the upper arms (caregiver ONLY).

⚠ **Warning! Do not** inject into skin that is within 5 cm of your belly button (navel), or is tender, damaged, bruised, or scarred.

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

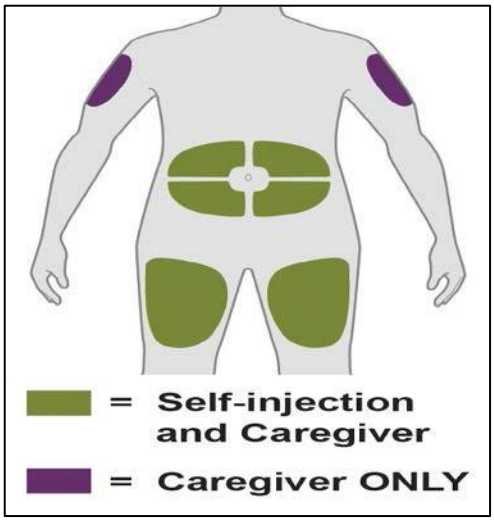

Figure E

6. Wash your hands.

a. Wash your hands with soap and water and dry them thoroughly (see *Figure F*).

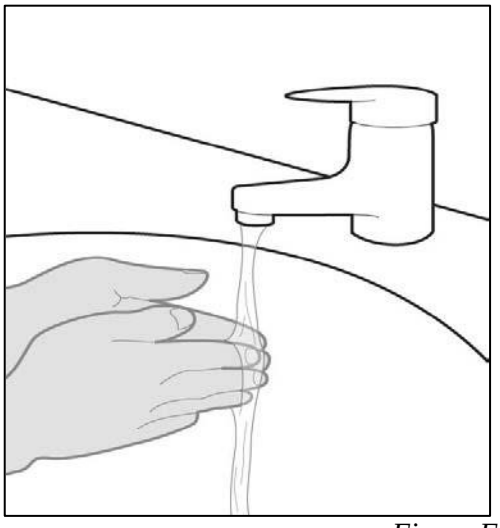

Figure F

7. Clean the injection site.

a. Clean the injection site with an alcohol swab (see *Figure G*).
b. Let the skin dry before injecting.

⚠ **Warning! Do not** blow on or touch the injection site again before giving the injection.

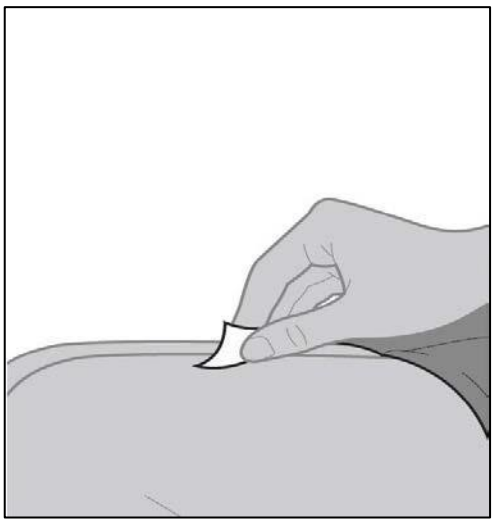

Figure G

Give the injection

8. Remove the Cap.

a. Pull the olive green Cap straight off and set it aside (see *Figure H*).

⚠ **Warning! Do not** remove the Cap until you are ready to inject.

⚠ **Warning! Do not** recap the Pen.

⚠ **Warning! Do not** touch the Needle Cover. Doing so may result in a needle stick injury.

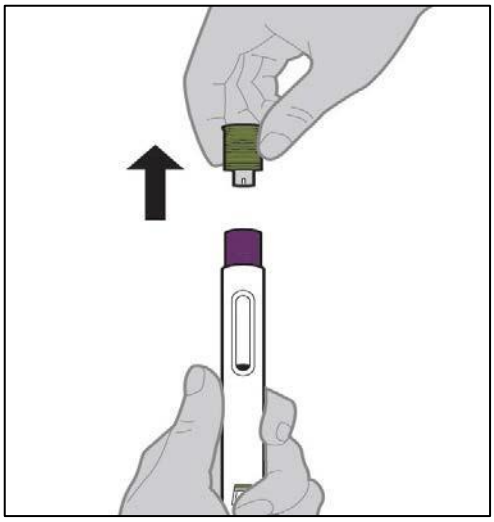

Figure H

9. Place the Pen on the injection site.

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 (see *Figure I*).

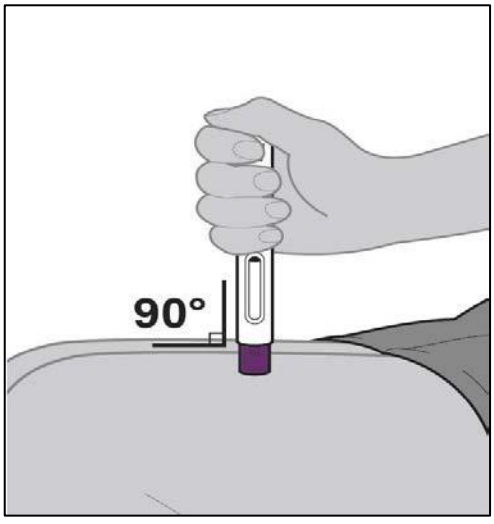

Figure I

10. Start the injection.

a. Press the Pen **firmly** against the skin (see *Figure J*).

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."

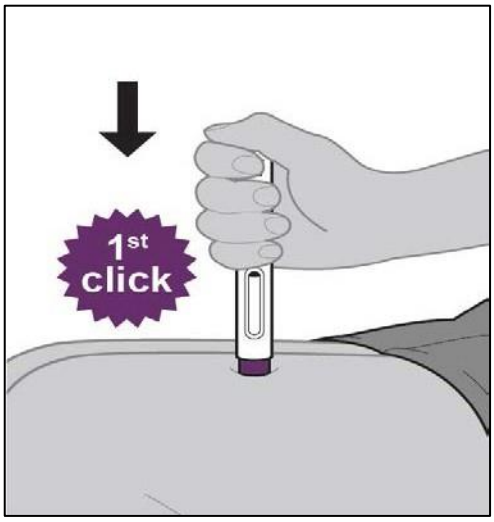

Figure J

11. Finish the injection.

a. After you hear the 2nd loud "click," continue to hold the Pen **firmly** against the skin and count slowly to five to ensure you inject the full dose (see *Figure K*).

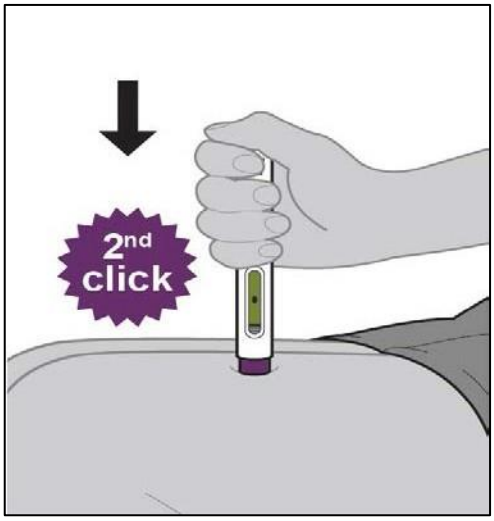

Figure K

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 L*).

⚠ **Warning! Do not** reuse the Pen.

⚠ **Warning! Do not** rub the injection site.

Note: After you remove the Pen from the injection site, the needle will be automatically covered (see Figure M).

Note: If the olive green Plunger Rod does not fill the Window completely, you did not receive your full dose. Call your healthcare provider immediately.

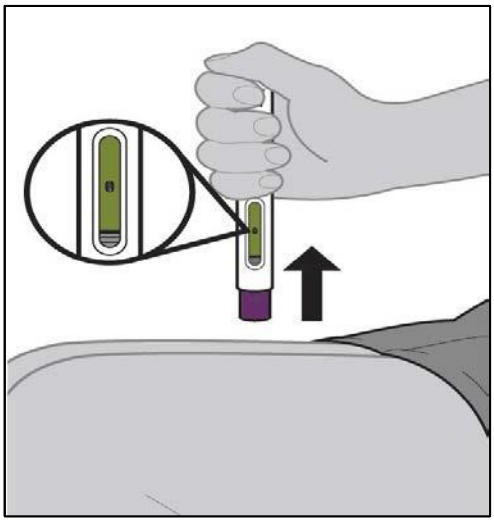

Figure L

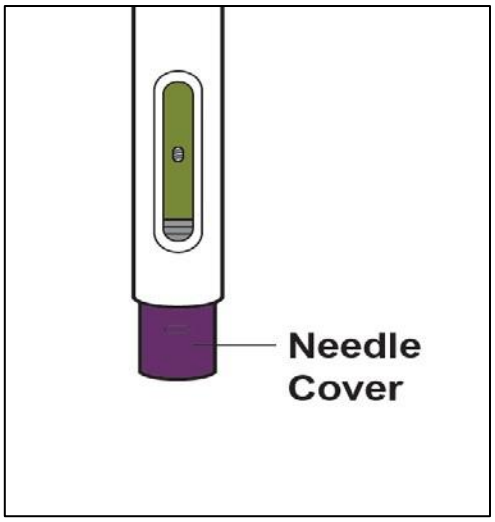

Figure M

After the injection

13. Dispose of the Pen.

a. Put the used Pen and the Cap in an approved sharps disposal container immediately after use (see *Figure N*).

⚠ **Warning! Do not** throw away (dispose of) the Pen in your household waste.

If you do not have an approved sharps disposal container, you may use a household container that is:

- made of a heavy-duty plastic;
- able to close with a tight-fitting, puncture-resistant lid, without sharps being able to come out;
- upright and stable during use;
- leak-resistant; and
- properly labelled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, it should be disposed of in accordance with local requirements.

Figure N

14. Care for the injection site.

a. Treat the injection site by gently pressing a cotton ball or gauze to the site and apply an adhesive bandage, if necessary.

Remsima SC

Infliximab

Patient Alert Card

Show this card to any doctor involved in your treatment.

This Patient Alert Card contains important safety information that you need to be aware of before and during treatment with Remsima.

Name patient:
Name doctor:
Telephone number doctor:

When starting a new card, please keep this card as a reference for 4 months after your last dose of Remsima.

Please read the Remsima 'Package Leaflet' carefully before you start using this medicine.

Date of Remsima therapy initiation:

Current administrations:

It is important that you and your doctor record the brand name and batch number of your medicine.

Brand name:
Batch number:

Ask your doctor to record the type and date of last screening(s) for tuberculosis (TB) below:

Test	Test
Date	Date
Result:	Result:

Please make sure you also have a list of all other medicines that you are using with you at any visit to a healthcare professional.

List of allergies

List of other medicines

Infections

Before treatment with Remsima

- Tell your doctor if you have an infection even if it is a very minor one.
- It is very important that you tell your doctor if you have ever had tuberculosis (TB), or if you have been in close contact with someone who has had TB. Your doctor will test you to see if you have TB. Ask your doctor to record the type and date of your last screening(s) for TB on the card.
- Tell your doctor if you have hepatitis B or if you know or suspect you are a carrier of the hepatitis B virus.

During treatment with Remsima

- Tell your doctor straight away if you have signs of an infection. Signs include a fever, feeling tired, (persistent) cough, shortness of breath, weight loss, night sweats, diarrhoea, wounds, dental problems, burning when urinating or 'flu-like' signs.

Heart Failure

Before treatment with Remsima

- Tell your doctor if you have any heart problems such as mild heart failure.

During treatment with Remsima

- Tell your doctor straight away if you notice signs of a heart problem. Signs include shortness of breath, swelling of the feet or changes in your heartbeat.

Pregnancy and Vaccinations

- In case you have received Remsima while you were pregnant, it is important that you inform your baby's doctor about it before your baby receives any vaccine. Your baby should not receive a 'live vaccine', such as BCG (used to prevent tuberculosis) within 6 months after birth.

Keep this card with you for 4 months after your last dose of Remsima, or in case of pregnancy, for at least 6 months after the birth of your baby. Side effects may occur a long time after your last dose.