READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

PR RENFLEXIS® (pronounced) <Ren-FLEK-sis>
(Infliximab for Injection)
Powder for Solution, Sterile, Lyophilized, 100 mg / vial

Read this carefully before you start taking **RENFLEXIS®** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **RENFLEXIS®**.

RENFLEXIS® is a biosimilar biologic drug (biosimilar) to the reference biologic drug Remicade®. A biosimilar is authorized based on its similarity to a reference biologic drug that was already authorized for sale.

Serious Warnings and Precautions

- Serious infections, including sepsis, tuberculosis, legionellosis (a serious form of bacterial pneumonia), listeriosis (an infection that usually develops after eating food contaminated by bacteria called listeria) and opportunistic infections (such as systemic fungal, viral, and bacterial infections), have been reported in patients, especially those 65 years and older, receiving infliximab for injection and other similar medicines. Some patients with these infections have died.
- Prior to treatment with RENFLEXIS®, you should tell your doctor if you have a chronic infection, a history of recurrent infection, or if you have lived in or traveled to an area where infections called histoplasmosis, coccidioidomycosis or blastomycosis are common. These infections are caused by fungus that can affect the lungs or other parts of your body. Ask your doctor if you don't know if these infections are common in the area in which you have lived or traveled. If you develop an infection during treatment with RENFLEXIS®, you should tell your doctor right away.
- Prior to treatment with RENFLEXIS®, you should tell your doctor if you have had tuberculosis, or if you have been exposed recently to anyone who might have tuberculosis, or if you have any other reason to believe you may be at risk for tuberculosis. Your doctor will evaluate you for tuberculosis and may begin treatment for tuberculosis before you are treated with RENFLEXIS®.
- Treatment with RENFLEXIS® must be interrupted if you develop a serious infection or sepsis. Tell your doctor if you have any symptoms of an infection (for example, fever, fatigue, cough, flu-like symptoms, or pain) while you are taking RENFLEXIS® and for 6 months after you receive the medicine. If you need surgery, tell your doctor that you have taken RENFLEXIS®.
- Lymphoma and other cancers, which may result in death, have been reported in children and teenage patients taking TNF-blockers, including infliximab for injection. Some patients who have received TNF-blockers, including infliximab for injection have developed a rare type of cancer called hepatosplenic T-cell lymphoma. Of these patients, most were teenage or young adult males and most had either Crohn's disease or ulcerative colitis. This type of cancer often results in death. Almost all patients had also received drugs known as azathioprine or 6-mercaptopurine in addition to TNF-blockers. You should also tell your doctor if you have had or develop lymphoma or other cancers while you are taking RENFLEXIS®.

What is RENFLEXIS® used for?

RENFLEXIS® is a medicine that is used in people with moderate to severe rheumatoid arthritis (in combination with methotrexate) and ankylosing spondylitis. Your doctor has chosen to treat your rheumatoid arthritis with RENFLEXIS® because you have moderately to severely active rheumatoid arthritis. Your doctor has chosen to treat your ankylosing spondylitis with RENFLEXIS® because you have had an inadequate response to other treatments or because you cannot tolerate other treatments.

RENFLEXIS® is also used in people with moderate to severe plaque psoriasis. Your doctor has chosen to treat your plaque psoriasis with RENFLEXIS® because your disease is still active even though you have tried other treatments.

RENFLEXIS® is also used in people with active psoriatic arthritis. Your doctor has chosen to treat your psoriatic arthritis with RENFLEXIS® because your disease is still active even though you have tried other treatments.

RENFLEXIS® is also used in adults, children and teenagers with moderate to severe Crohn's disease or with moderate to severe ulcerative colitis. Your doctor has chosen to treat your Crohn's disease or ulcerative colitis with RENFLEXIS® because your disease is still active even though you have tried other treatments.

How does RENFLEXIS® work?
Research has shown that in these diseases the body overproduces a substance known as tumour necrosis factor alpha (TNF alpha). The active ingredient in RENFLEXIS® is called infliximab. Infliximab is a monoclonal antibody, a type of protein that recognises and binds to other unique proteins. Infliximab binds to and neutralises TNF alpha. Infliximab is made from mouse and human proteins.

Improvement may be seen within several weeks of infliximab for injection treatment, sometimes as early as 2 weeks after starting infliximab for injection. According to clinical trial data, full effect was usually seen around 3 months and was generally sustained with continued treatment.

RENFLEXIS® is a medicine that affects your immune system. RENFLEXIS® can lower the ability of your immune system to fight infections.

What are the ingredients in RENFLEXIS®?
Medicinal ingredients: Infliximab
Non-medicinal ingredients: Sucrose, polysorbate 80, monobasic sodium phosphate monohydrate and dibasic sodium phosphate heptahydrate

RENFLEXIS® comes in the following dosage forms:
RENFLEXIS® is supplied as lyophilized concentrate for IV injection in individually-boxed single-use vials of 100 mg infliximab for injection.

Vial stopper is free of natural rubber latex.

Do not use RENFLEXIS® if:
- If you have a severe infection, such as sepsis (an infection in the bloodstream), abscess, tuberculosis or other serious infection, you must not take RENFLEXIS®.
- If you have heart failure that is moderate or severe, you must not take RENFLEXIS®.
- If you are allergic to infliximab for injection or any ingredient in RENFLEXIS® (polysorbate 80, sodium phosphate and sucrose), or if you have a history of allergies to mouse proteins, you should not take RENFLEXIS®.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take RENFLEXIS®. Talk about any health conditions or problems you may have, including if you have:

- congestive heart failure: If you have mild heart failure and you are being treated with RENFLEXIS®, your heart failure status must be closely monitored by your doctor. If you develop new or worsening symptoms of heart failure (such as shortness of breath or swelling of your feet), you must contact your doctor immediately.
- other heart problems: Some patients have experienced a heart attack (some of which led to death), low blood flow to the heart, or abnormal heart rhythm within 24 hours of beginning their infusion of RENFLEXIS®. Symptoms may include chest discomfort or pain, arm pain, stomach pain, shortness of breath, anxiety, lightheadedness, dizziness, fainting, sweating,

nausea, vomiting, fluttering or pounding in your chest, and/or a fast or a slow heartbeat. Tell your doctor right away if you have any of these symptoms

- immediate allergic reactions: Some patients who have received infliximab for injection have developed allergic reactions, including anaphylaxis. Some reactions can happen while you are getting your infusion or shortly afterwards. Some of these reactions have been serious. The symptoms include hives, difficulty breathing, pain and high or low blood pressure. Your doctor may decide to stop RENFLEXIS® treatment for severe reactions. Your doctor can prescribe medicines to treat these effects.
- delayed allergic reactions: Some allergic reactions can occur 3 to 12 days after RENFLEXIS® retreatment. The symptoms of this type of delayed reaction include muscle or joint pain with fever or rash. Tell your doctor if you notice any of these symptoms.
- nervous system diseases: Tell your doctor if you have a disease that affects your nervous system, like multiple sclerosis, neuropathies, Guillain-Barré syndrome, or seizures, or you have been diagnosed with optic neuritis, or if you experience any numbness, tingling, or visual disturbances. Some patients have reported that their nervous system disease got worse after receiving infliximab for injection.
- autoimmune disease: Some patients treated with infliximab for injection have developed symptoms that suggest an autoimmune disease called lupus-like syndrome. Tell your doctor if you notice symptoms of lupus-like syndrome, such as, prolonged chest discomfort or pain, shortness of breath, joint pain, or sun-sensitive rash on the cheeks or arms. Your doctor will evaluate your condition and may decide to stop your treatment with RENFLEXIS®.
- liver injury: There have been cases where people taking infliximab for injection have developed liver problems. Signs that you could be having a problem include: jaundice (skin and eyes turning yellow), dark brown-colored urine, right-sided abdominal pain, fever, and severe fatigue (tiredness). You should contact your doctor immediately if you develop any of these symptoms.
- previous phototherapy: Tell your doctor if you have had phototherapy (treatment with ultraviolet light or sunlight along with a medicine to make your skin sensitive to light) for psoriasis. In clinical trials, skin cancers were more common in patients who received prior phototherapy.
- blood Problems: In some instances, patients treated with TNF-blocking agents may develop low blood counts, including a severely decreased number of white blood cells. If you develop symptoms such as persistent fever or infections, bleeding, or bruising, you should contact your doctor right away.
- stroke: Some patients have experienced a stroke within approximately 24 hours of their infusion of RENFLEXIS®. Tell your doctor right away if you have symptoms of a stroke which may include: numbness or weakness of the face, arm or leg, especially on one side of the body; sudden confusion, trouble speaking or understanding; sudden trouble seeing in one or both eyes, sudden trouble walking, dizziness, loss of balance or coordination or a sudden, severe headache.
- hepatitis B: Treatment with TNF-blocking agents such as infliximab for injection may result in a reactivation of the hepatitis B virus in people who carry this virus. If you have or have had hepatitis B infection or know or suspect you may be a carrier of hepatitis B virus, be sure to tell your doctor about this as this may impact the decision to start or continue treatment with RENFLEXIS®. Your doctor should do a blood test for hepatitis B virus before you start treatment with RENFLEXIS®.
- vaccination: Tell your doctor that you have received RENFLEXIS® if you need to get a vaccination. It is not known if medicines like RENFLEXIS® can interfere with vaccinations. You should not receive live vaccines while you are taking RENFLEXIS®. The use of a ‘live’ vaccine may result in an infection caused by the ‘live’ vaccine or bacteria contained in the

vaccine (when you have a weakened immune system). It is recommended that you be brought up to date with all vaccinations guidelines prior to starting RENFLEXIS®.

- therapeutic infectious agents: Tell 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).
- pregnancy, breast-feeding and ability to have children: If you are being treated with RENFLEXIS®, you must avoid becoming pregnant by using adequate contraception during your treatment and for 6 months after your last RENFLEXIS® injection. Tell your doctor if you think you may be pregnant, are breastfeeding, or planning to conceive a child. Your doctor will help you decide whether or not to use RENFLEXIS®. If you have a baby and you were using RENFLEXIS® during your pregnancy, it is important to tell your baby's doctor and other healthcare professionals about your RENFLEXIS® use so they can decide when your baby should receive their vaccinations, including live vaccines, such as BCG (used to prevent tuberculosis).
  If you received RENFLEXIS® while you were pregnant, your baby may be at higher risk for getting an infection. It is important that you tell your baby's doctors and other health care professionals about your RENFLEXIS® use before the baby receives any vaccine. Administration of BCG vaccine within 6 months after birth to the baby whose mother received RENFLEXIS® while pregnant may result in infection in the newborn with severe complications, including death. For other types of vaccines, discuss with your doctor. Breast feeding is not recommended during treatment and for 6 months after the last dose of RENFLEXIS®. Your doctor will help you decide whether or not to use RENFLEXIS®.
  Severely decreased numbers of white blood cells have also been reported in infants born to women treated with RENFLEXIS® during pregnancy. If your baby has continual fevers or infections, contact your baby's doctor immediately.
  It is not known if RENFLEXIS® can affect your ability to have children in the future.

Other warnings you should know about:
Reports of a type of blood cancer called lymphoma in patients on infliximab for injection or other TNF-blockers are rare but occur more often than expected for people in general. People who have been treated for rheumatoid arthritis, Crohn's disease or ankylosing spondylitis for a long time, particularly those with highly active disease may be more prone to develop lymphoma.

Cancers, other than lymphoma, have also been reported. There have been cases of cancers, including unusual types, in children and teenage patients taking TNF-blocking agents, which sometimes resulted in death. For children and adults taking TNF-blocker medicines, the chances of getting lymphoma or other cancers may increase.

Some patients treated with infliximab for injection have developed certain kinds of skin cancer. If any changes in the appearance of the skin or growths on the skin occur during or after therapy, tell your doctor.

Some women being treated for rheumatoid arthritis with infliximab for injection have developed cervical cancer. For women taking RENFLEXIS®, including those over 60 years of age, your doctor may recommend that you continue to be regularly screened for cervical cancer.

Patients with a specific type of lung disease called COPD (Chronic Obstructive Pulmonary Disease) may be at increased risk for cancer with RENFLEXIS® treatment. If you have COPD you should discuss with your doctor whether RENFLEXIS® is appropriate for you.

Tell your healthcare professional about all the medicines you take, including any drugs,

vitamins, minerals, natural supplements or alternative medicines.

The following may interact with RENFLEXIS®:

- Tell your doctor about all medicines that you have recently taken or are taking during your treatment with RENFLEXIS®. These include any other medicines to treat Crohn's disease, ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis or psoriasis. Drugs that may interact with RENFLEXIS® include: prescription and non-prescription medicines, vitamins, and herbal supplements.

- Patients with rheumatoid arthritis or Crohn's disease often take other medicines that can cause side effects. Special studies have not been done to determine whether other medicines will react with RENFLEXIS®. In studies of RENFLEXIS, patients were also taking antibiotics, antivirals, corticosteroids, mercaptopurine (6MP), azathioprine (AZA), methotrexate (MTX), and aminosalicylates along with RENFLEXIS®. Patients who took immunosuppressants, such as methotrexate, corticosteroids, mercaptopurine, azathioprine, had a lower risk of allergic reactions during infusion.

- Tell your doctor if you take KINERET® (anakinra) or ORENCIA® (abatacept). RENFLEXIS® should not be taken together with anakinra or abatacept.

- If you have a baby while you are using RENFLEXIS®, tell your baby's doctor about your RENFLEXIS® use before the baby receives any live vaccines.

How to take RENFLEXIS®:

RENFLEXIS® will be given to you by a healthcare professional. The medicine will be given to you through a needle placed in a vein in your arm. This is called an infusion. If you have Crohn's disease, ulcerative colitis, ankylosing spondylitis, psoriatic arthritis, or plaque psoriasis, the infusion will take about 2 hours. If you have rheumatoid arthritis, the first 3 infusions will be given to you over a period of about 2 hours, after the third infusion your doctor may decide to give you the infusion over a 1 hour period. During the infusion you will be monitored for side effects. You must stay for 1 to 2 hours after the infusion so that you can continue to be watched for any reactions to the medicine.

Your doctor may ask you to take other medicines along with RENFLEXIS®.

Where I may receive the infusion:

Your doctor will decide where you will receive the infusion. The Organon Harmony® Infusion Network has been established to facilitate the administration of RENFLEXIS®. This network consists of clinics located across Canada that are staffed by qualified healthcare professionals specially trained in the administration of RENFLEXIS® infusions. Contact your doctor if you have any questions.

Information about the Organon Harmony® Infusion Network can be obtained by contacting Organon Harmony® at: 1-866-556-5663

Usual dose:

<u>Rheumatoid Arthritis</u>

The recommended dose of RENFLEXIS® (infliximab for injection) is 3 mg/kg given as an intravenous infusion followed by additional 3 mg/kg doses at 2 and 6 weeks after the first infusion then every 8 weeks thereafter. RENFLEXIS® should be given in combination with methotrexate.

Ankylosing Spondylitis
The recommended dose of RENFLEXIS® is one initial infusion of 5mg/kg followed by infusions of 5mg/kg at 2 and 6 weeks after the first dose. Then you will receive an infusion every 6 to 8 weeks thereafter.

Crohn's Disease and Fistulising Crohn's Disease
Adults
The recommended dose of RENFLEXIS® is 5 mg/kg given as an induction regimen at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 8 weeks thereafter for the treatment of moderate to severe, active Crohn's disease. For patients who have an incomplete response, consideration may be given to adjusting the dose up to 10 mg/kg. Your doctor may consider doing a blood test (therapeutic drug monitoring) to determine how much infliximab for injection is in your blood stream in order to optimize your dose of RENFLEXIS®.
Children (9 years of age or older)
The recommended dose of RENFLEXIS® for children with moderately to severely active Crohn's disease is 5 mg/kg given as an induction regimen of 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 8 weeks.

Ulcerative Colitis
Adults
If you are receiving RENFLEXIS® for ulcerative colitis, you will receive your first 5 mg/kg dose followed by additional 5 mg/kg doses at 2 and 6 weeks after the first dose. You will then receive a dose every 8 weeks thereafter. Your doctor will monitor your response to RENFLEXIS® and may change your dose. Your doctor may consider doing a blood test (therapeutic drug monitoring) to determine how much infliximab for injection is in your blood stream in order to optimize your dose of RENFLEXIS®.

Children (6 years of age or older)
The recommended dose of RENFLEXIS® for children with moderately to severely active ulcerative colitis is 5 mg/kg given as an induction regimen of 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 8 weeks.

Psoriatic Arthritis
The recommended dose of RENFLEXIS® is 5 mg/kg as an intravenous infusion followed with additional doses at 2 and 6 weeks after the first infusion then every 8 weeks thereafter. If you show no response at 24 weeks, no additional treatment with RENFLEXIS® should be given.

Plaque Psoriasis
The recommended dose of RENFLEXIS® is 5 mg/kg given as an intravenous infusion followed with additional 5 mg/kg doses at 2 and 6 weeks after the first infusion then every 8 weeks thereafter. If you do not show an adequate response at Week 14, after infusions at Weeks 0, 2, and 6, no additional treatment with RENFLEXIS® should be given.

Overdose:
Single doses up to 20 mg/kg have been administered without any direct toxic effect. In case of overdosage, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions or effects and appropriate symptomatic treatment instituted immediately.

If you think you have taken too much RENFLEXIS®, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:
If you forget or miss an appointment to receive RENFLEXIS®, make another appointment as soon as possible to find out when to receive your next dose of RENFLEXIS®.

What are possible side effects from using RENFLEXIS®?
These are not all the possible side effects you may feel when taking RENFLEXIS®. If you experience any side effects not listed here, contact your healthcare professional. Please also see Warnings and Precautions.

Some patients had side effects that caused them to stop RENFLEXIS® treatment. The most common reasons were shortness of breath, rash, and headache.

Other common side effects besides the ones already mentioned in this leaflet include abdominal pain, back pain, coughing, diarrhea, dizziness, fatigue, itchiness, pain, upper respiratory infections (such as bronchitis, sinusitis, cold, sore throat), upset stomach, and urinary tract infections. RENFLEXIS® may have a minor influence on the ability to drive and use machines. Dizziness may occur following administration of RENFLEXIS®.

Children and teenagers who took infliximab for injection in studies for ulcerative colitis had similar side effects as adults with ulcerative colitis. The most common side effects observed in children with ulcerative colitis include: cough and cold symptoms including sore throat, stomach pain, fever, headache and anemia (low red blood cell count). Among patients who took infliximab for injection for ulcerative colitis in clinical studies, more children had infections as compared with adults, including bladder infections, skin infections, and bronchitis.

Some of the side effects of RENFLEXIS® can be serious and may require treatment.

Tell your doctor if you experience any of the effects listed in this leaflet or any other side effects.

Serious side effects and what to do about them				
Symptom / effect		Talk to your healthcare professional		Stop taking drug and get immediate medical help
		Only if severe	In all cases	
COMMON	Serious infections: symptoms of fever, feel very tired, have a cough or develop flu-like symptoms or develop an abscess.		✓	
	Allergic reactions: symptoms, while you are getting your RENFLEXIS® infusion or shortly afterwards, of hives (red, raised, itchy patches of skin), difficulty breathing, chest pain and high or low blood pressure or symptoms 3 to 12 days after receiving		✓	

	RENFLEXIS® including fever, rash, headache and muscle or joint pain.			
Uncommon	Liver injury: signs that you could be having a problem include: jaundice (skin and eyes turning yellow), dark brown-colored urine, right sided abdominal pain, fever and severe fatigue (tiredness).		✓	
	Heart failure: If you have been told that you have a heart problem called congestive heart failure, you will need to be closely monitored by your doctor. New or worse symptoms that are related to your heart condition, including shortness of breath or swelling of your ankles or feet.		✓	
	Blood problems: symptoms of fever that doesn't go away, bruising or bleeding very easily or looking very pale.		✓	
	Nervous system disorders: signs include changes in your vision (including blindness), seizures, weakness in your arms and/or legs, and numbness or tingling in any part of your body.		✓	
	Malignancy: if you have had or develop lymphoma or other cancers, including skin cancers, while you are taking RENFLEXIS®.		✓	
	Lupus: symptoms may include chest discomfort or pain that doesn't go away, shortness of breath, joint pain, or a		✓	

	rash on the cheeks or arms that gets worse in the sun.			
Rare	Skin problems: skin rashes including redness, itching, skin peeling and blistering; Small pus-filled bumps that can spread over the body, sometimes with a fever (acute generalized exanthematous pustulosis); Itchy reddish-purple skin rash and/or threadlike white-grey lines on mucous membranes (lichenoid reactions)		✓	
	Lung problems: symptoms of new or worsening shortness of breath.		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

This is not a complete list of side effects. For any unexpected effects while taking RENFLEXIS®, contact your doctor or pharmacist.

Reporting Side Effects

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at MedEffect;
- By calling 1-866-234-2345 (toll-free);
- By completing a Patient Side Effect Reporting Form and sending it by:
  - Fax to 1-866-678-6789 (toll-free), or
  - Mail to: Canada Vigilance Program
    Health Canada, Postal Locator 1908C
    Ottawa, ON
    K1A 0K9

  Postage paid labels and the Patient Side Effect Reporting Form are available at MedEffect.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

RENFLEXIS® must be stored in the original package in the refrigerator before use.
It must be kept out of the reach and sight of children.
The vial must be kept sealed. Only a healthcare professional should prepare the medicine before use and administer it to you. It should not be used beyond the expiration date.

If you want more information about RENFLEXIS®:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://www.canada.ca/en/health-canada.html); the Canadian distributor (Organon Canada)'s website www.organon.ca, or by calling the Canadian distributor (Organon Canada) at
  1-844-820-5468.

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