PATIENT INFORMATION LEAFLET (PIL))

SCHEDULING STATUS
Schedule 4

REVELLEX® 100 mg

Powder for concentrate for solution for infusion

Infliximab

Contains sugar (sucrose).

Each vial contains 500 mg sucrose.

Read all of this leaflet carefully before you start using REVELLEX

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- REVELLEX has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What REVELLEX is and what it is used for
2. What you need to know before you use REVELLEX
3. How to use REVELLEX
4. Possible side effects
5. How to store REVELLEX
6. Contents of the pack and other information

1. What REVELLEX is and what it is used for

REVELLEX is intended for the treatment in adults of rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, Crohn's disease and ulcerative colitis, with the aim to reduce inflammatory activity. It is also used in children 6 years of age and older for Crohn's disease and ulcerative colitis.

In these diseases, the body produces too much of a substance called tumor necrosis factor alpha (TNF-alpha). Too much of this substance causes your body's immune system to attack healthy tissue and result in inflammation. Blocking TNF-alpha with REVELLEX can reduce inflammation but can also reduce your immune system's ability to fight off infections. Your doctor has decided to treat you with REVELLEX because your disease is still active even though you have tried other treatments.

2. What you need to know before you use REVELLEX

Do not use REVELLEX

- If you are hypersensitive (allergic) to infliximab or to any murine (mouse) proteins or any of the other ingredients of REVELLEX listed in section 6.
- if you have a severe infection, including tuberculosis. It is important that you tell your doctor if you have symptoms of infection e.g. fever, malaise, wounds and dental problems.
- if you have moderate or severe heart failure. It is important to tell your doctor if you have had or have a serious heart condition.

Warnings and precautions

- **Infections:**

Tell your doctor if you have an infection even if it is a very minor one before you are given REVELLEX. Tell your doctor if you have lived in or travelled to an area where infections called histoplasmosis, coccidiomycosis, or blastomycosis are common before you are given REVELLEX. 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 REVELLEX. If you are 65 years of older, you have a greater risk. These infections may be serious and include tuberculosis, infections caused by viruses, fungi or bacteria, or other opportunistic infections and sepsis that may be life threatening.

Tell your doctor straight away if you get signs of infection during treatment with REVELLEX. Signs include fever, cough, flu-like symptoms, feeling unwell, red or hot skin, wounds or dental problems. Your doctor may recommend temporary discontinuation of REVELLEX.

- **Tuberculosis (TB):**

It is very important that you tell your doctor if you have ever had tuberculosis, or if you have been in close contact with someone who has or had tuberculosis. Your doctor will test you to see if you have tuberculosis. Cases of TB have been reported in patients treated with REVELLEX. Even in patients who have been treated with medications for TB. If your doctor feels that you are at risk for tuberculosis, you may be treated with medicines for tuberculosis before you begin REVELLEX therapy. Tell your doctor straight away if you get signs of TB during treatment with REVELLEX. Signs include persistent cough, weight loss, tiredness, fever, night sweats.

- **Hepatitis B Virus (HBV):** Tell your doctor if you know or suspect you are a carrier

of this virus, if you have active hepatitis B or if you think you think you might be at risk of contracting hepatitis B. Your doctor should test you for HBV. Treatment with TNF blockers such as REVELLEX may result in reactivation of hepatitis B virus in patients who carry this virus, which can be life-threatening in some cases.

- **Cancer/Lymphoma:** Tell your doctor before you are given REVELLEX 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 than average risk of developing lymphoma.

  Children and adults taking REVELLEX may have an increased risk of developing lymphoma or another cancer.

  Some patients who have received TNF-blockers, including REVELLEX 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 REVELLEX 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 REVELLEX have developed cervical cancer. For women taking REVELLEX including those over 60 years of age, your doctor may recommend that you continue to be regularly screened for cervical cancer.

- **Lung disease or heavy smoking:** Tell your doctor before you are given REVELLEX if you have a lung disease called Chronic Obstructive Pulmonary Disease (COPD) or if you are a heavy smoker. Patients with COPD and/or patients who are heavy smokers may have a higher risk of developing cancer with REVELLEX treatment.

- **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 REVELLEX. Signs include shortness of breath or swelling of your feet.

- **Neurological disease:** Tell your doctor if you have or ever have had a problem that affects your nervous system before you are given REVELLEX. 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 REVELLEX. 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 REVELLEX.

- **Vaccinations:** If you have a baby while you are using REVELLEX, tell your baby's doctor about the REVELLEX use before the baby received any vaccine, including live vaccine, such as the BCG vaccine (used to prevent tuberculosis), rotavirus vaccine, or any other live vaccines. For more information see section on Pregnancy and lactation. **If you are breastfeeding, it is important that you tell your baby's doctors and other healthcare professionals about your REVELLEX use before**

your baby is given any vaccine.

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

- **Immune system disorder:** Some patients receiving REVELLEX have developed symptoms of an immune system disorder called lupus. Tell your doctor straight away if you develop symptoms of lupus during treatment with REVELLEX. Signs include joint pain or a rash on cheeks and arms that is sensitive to the sun.

- **Had treatment with REVELLEX before:** Tell your doctor if you have had treatment with REVELLEX in the past and are now starting REVELLEX treatment again. If you had a break in your REVELLEX treatment for more than 16 weeks, there is a higher risk for allergic reactions when you start treatment again.

- **Operations or dental procedures:** Tell your doctor if you are going to have any operations or dental procedures.

- **Liver problems**: Some patients receiving REVELLEX have developed serious liver problems. Tell your doctor straight away if you get symptoms of liver problems during treatment with REVELLEX. Signs include yellowing of the skin and eyes, dark-brown coloured urine, pain or swelling in the upper right side of the stomach area, joint pain, skin rashes, or fever.

- **Low blood counts**: In some patients receiving REVELLEX, 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 REVELLEX. Signs include persistent fever, bleeding or bruising more easily, small red or purple spots caused by bleeding under the skin, or looking pale.

Children

- **Children and adolescents**: The information above also applies to children and adolescents in addition:
    - Some children and teenage patients who have received TNF-blockers such as REVELLEX have developed cancers, including unusual types, which sometimes resulted in death.
    - More children taking REVELLEX developed infections compared to adults.
    - Children should receive recommended vaccinations before starting REVELLEX treatment. Children may receive some vaccines during treatment but should not receive live vaccines while using REVELLEX.

Other medicines and REVELLEX

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines).

In studies of REVELLEX, patients were taking other medications along with REVELLEX for the treatment of their disease. Tell your doctor if you are taking or have recently taken other medications before and during treatment with REVELLEX. These include any other medicines to treat Crohn's disease, ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis or psoriasis. Also tell your doctor if you plan to take other medications.

Especially, tell your doctor or pharmacist if you take anakinra or abatacept. REVELLEX should not be taken together with anakinra or abatacept. Also tell your doctor or pharmacist if you are taking any other medicines that affect your immune system.

While using REVELLEX you should not receive live vaccines. If you have a baby or if you are breastfeeding while you are using REVELLEX, tell your baby's doctor about your REVELLEX use before the baby receives any live vaccines. If possible, you should have all of your vaccines brought up to date before starting treatment with REVELLEX.

REVELLEX with food and drink

REVELLEX can be used with or without food or drink.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before using this medicine.

If you have a baby while you are using REVELLEX, it is important to tell your baby's doctor and other healthcare professionals about your REVELLEX use so they can decide when your baby should receive their vaccinations.

If you received REVELLEX while you were pregnant, your baby may be at higher risk for getting an infection. It is important to tell your baby's doctor and other healthcare professionals about your REVELLEX use before the baby receives any vaccine, including live vaccines as the BCG (used to prevent tuberculosis), rotavirus vaccine, or any other live vaccines. Administration of BCG vaccine within 12 months after birth to the day whose mother received REVELLEX while pregnancy may result in infection in the

newborn with severe complications, including death. For other type of vaccines, discuss with your doctor.

If you are breast-feeding, it is important that you tell your baby's doctors and other healthcare professionals about your REVELLEX use before your baby is given any vaccine. Live vaccines should not be given to your baby while you are breast-feeding unless your baby's doctor recommends otherwise.

Severely decreased numbers of white blood cells have also been reported in infants born to women treated with REVELLEX during pregnancy. If your baby has continual fevers or infections, contact your baby's doctor immediately.

Driving and using machines

It is not expected that REVELLEX will affect your ability to drive or use machines. If you feel tired or unwell after having REVELLEX, do not drive or use any tools or machines.

REVELLEX contains sucrose

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before using REVELLEX.

REVELLEX contains sugar (sucrose) which may have an effect on the control of your blood sugar if you have diabetes mellitus.

3. How to use REVELLEX

Do not share medicines prescribed for you with any other person.

Always use REVELLEX exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Your doctor will tell you how long your treatment with REVELLEX will last. Do not stop treatment early because your symptoms may return. If you have the impression that the effect of REVELLEX is too strong or too weak, tell your doctor or pharmacist.

REVELLEX will be prepared and given to you by a healthcare professional.

REVELLEX is administered as an intravenous infusion, which means that the medicine will be administered to you through a needle placed in a vein in your arm. If you have Crohn's disease, ulcerative colitis, ankylosing spondylitis, psoriatic arthritis, or psoriasis, the infusion will be given to you over a period of 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 your REVELLEX over a 1 hour period. During the infusion and for a period of time after you receive REVELLEX, you will be monitored for side effects. Your doctor may ask you to take other medications along with REVELLEX.

The doctor will decide your dose (mg) and how often you will be given REVELLEX. This will depend on your disease, weight and how well you respond to REVELLEX.

Crohn's disease or Fistulising Crohn's disease

If you are an adult, child or teenager and have Crohn's disease or fistulising Crohn's disease, you will receive a dose of REVELLEX followed by additional doses at 2 and 6 weeks after the first dose. You will then receive a dose every 8 weeks. Your doctor will monitor your response to REVELLEX and may adjust your dose.

Ulcerative colitis

If you are an adult, child or teenager and have ulcerative colitis, you will receive a dose of REVELLEX followed by additional doses at 2 and 6 weeks after the first dose. You will

then receive a dose every 8 weeks. Your doctor will monitor your response to REVELLEX and if you are an adult, may adjust your dose.

Rheumatoid arthritis

If you have rheumatoid arthritis, you will initially receive three doses of REVELLEX. The first dose will be followed by doses at 2 and 6 weeks after the first dose. You will then receive a dose every 8 weeks. Your doctor will monitor your response to REVELLEX and may adjust your dose or dose you more frequently (as often as every 4 weeks). Your doctor will also give you methotrexate or you will need to continue taking it.

Ankylosing Spondylitis

If you have ankylosing spondylitis you will initially receive three doses of REVELLEX. The first dose will be followed by doses at 2 and 6 weeks after the first dose. You will then receive a dose every 6 weeks.

Psoriatic arthritis

If you have psoriatic arthritis you will initially receive three doses of REVELLEX. The first dose will be followed by doses at 2 and 6 weeks after the first dose. You will then receive a dose every 8 weeks.

Psoriasis

If you have psoriasis you will initially receive three doses of REVELLEX. The first dose will be followed by doses at 2 and 6 weeks after the first dose. You will then receive a dose every 8 weeks.

Use in children and adolescents

REVELLEX should only be used in children if they are being treated for Crohn's disease or ulcerative colitis. The children must be 6 years of age or older.

If you administer more REVELLEX than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, seek help at the nearest hospital or poison control centre.

Since the healthcare professional will administer REVELLEX, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you forget to administer REVELLEX

If you forget or missed an appointment to receive REVELLEX, make another appointment as soon as possible.

4. Possible side effects

REVELLEX can have side effects. Not all side effects reported for REVELLEX are included in this leaflet. Should your general health worsen or if you experience any untoward effects while using REVELLEX, please consult your health care provider for advice.

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. Some of these reactions may be serious or life-threatening. An allergic reaction could happen within 2 hours of your injection or later. More signs of an allergic reaction that may happen 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, light-headedness, dizziness, fainting, sweating, nausea (feeling sick), vomiting, fluttering or pounding in your chest, a fast or a slow heartbeat, and/or 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, collection of pus in the gut or around the anus (abscess), dental problems or burning sensation when urinating.
- **Possible signs of cancer** including but not limited to swelling of lymph nodes, weight loss, fever, unusual skin nodules, changes in moles or skin colouring, or unusual vaginal bleeding.
- **Signs of a lung problem** such as coughing, breathing difficulties or tightness in the chest.
- **Signs of 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 eyesight such 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, pain or swelling in the upper right side of the stomach area, joint pain, skin rashes, or fever.
- **Signs of immune system disorder** 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 the mouth, throat, nose, genitals and eyes or small pus-filled bumps that can spread over the body. These skin reactions can be accompanied by fever.

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

The following side effects have been observed with REVELLEX:

Frequent side effects:

- Stomach pain, feeling sick
- Viral infections such as herpes or flu
- Upper respiratory infections such as sinusitis
- Headache
- Side effect due to an infusion
- Pain
- Changes in how your liver works, increase in liver enzymes (shown in blood tests)
- Lung or chest infections such as bronchitis or pneumonia
- 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 infections of the skin (cellulitis)
- Infections of the skin due to a fungus
- 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.

Less frequent side effects:

- Shortage of blood supply, swelling of a vein
- Collection of blood outside the blood vessels (haematoma) or bruising
- Skin problems such as blistering, warts, abnormal skin colouration or pigmentation, or swollen lips, or thickening of the skin, or red, scaly, and flaky skin
- Severe allergic reactions (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 or 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 feels worse with breathing (pleurisy)
- Tuberculosis
- Kidney infections
- Low platelet count, too many white blood cells
- Infections of the vagina
- Blood test showing “antibodies” against your own body
- A type of blood cancer (lymphoma)
- Your body 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
- Inflamed liver caused by a problem with the immune system (autoimmune hepatitis)
- Liver problem that causes yellowing of the skin or eyes (jaundice)
- Abnormal tissue swelling or growth
- Several allergic reaction that may cause loss of consciousness and could be life-threatening
- Swelling of small blood vessels (vasculitis)

- Immune disorders that could affect the lungs, skin and lymph nodes (such as sarcoidosis)
- Collection 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 or acute generalised exanthematous pustulosis
- Other skin problems such as erythema multiforme, lichenoid reactions (itchy reddish-purple skin rash and/or threadlike white-grey lines on mucous membranes), 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
- Problems with the nerves behind the eye, which may lead to painful and limited eye movements, loss of feeling in the forehead and vision loss (orbital apex syndrome)
- Fluid in the lining of the heart (pericardial effusion)
- Serious lung problems (such as intestinal 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 under the skin
- Abnormal values of a blood protein called “complement factor” which is part of the immune system
- Cancer in children and adults
- A rare blood cancer affecting most young people (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 infusion
- Infection due to alive vaccine because of a weakened immune system.

Additional side effects in children and adolescents

Children who took REVELLEX for Crohn's disease showed some differences in side effects compared with adults who took REVELLEX for Crohn's disease. The side effects that happened more in children were: low red blood cells (anaemia), blood in stool, low overall levels of white blood cells (leucopenia), redness or blushing (flushing), viral infections, low levels of white blood cells that fight infection (neutropenia), bone fracture, bacterial infection and allergic reactions of the breathing tract.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist or nurse. You can also report side effects to SAHPRA via the **"6.04 Adverse Drug Reaction Reporting Form"** found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of REVELLEX.

5. How to store REVELLEX

Store all medicine out of reach of children.

Store all medicines out of sight of children.

Store at 2 to 8 °C (in a refrigerator).

It can also be stored in the original carton outside of refrigerated storage up to a maximum of 30 °C for a single period of up to 6 months. In this situation, do not return to refrigerated storage again. Write the new expiration date on the carton, including day/month/year. This new expiration date should not exceed the original 36 months expiry date printed on the carton. Discard the medicine if not used by the new expiration date or the expiration date printed on the carton, whichever is earlier.

The infusion should be started within 3 hours of preparation.
Your doctor or other healthcare professionals will take care of handling and storing REVELLEX. REVELLEX will not be given to you if there are opaque particles, discolouration or other foreign particles present.

6. Contents of the pack and other information

What REVELLEX contains

The active substance is infliximab. Each vial contains 100 mg of infliximab. After preparation each mL contains 10 mg of infliximab.
The other ingredients are dibasic sodium phosphate, monobasic sodium phosphate, polysorbate 80 and sucrose.

What REVELLEX looks like and contents of the pack

REVELLEX is supplied as a lyophilised powder in individually-boxed single-use glass vials with rubber stoppers and aluminium crimps protected by plastic caps.
The powder is a freeze-dried white pellet.

Holder of certificate of registration

JANSSEN PHARMACEUTICA (Pty) Ltd

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Access to the corresponding Professional Information:

Included in the carton, accompanying this patient information leaflet.

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