FINAL PATIENT INFORMATION LEAFLET

(Clean copy)

SCHEDULING STATUS

Schedule 4

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM

REVELLEX® 100 mg Injection

Powder for concentrate for solution for infusion

Active substance: Infliximab

Read all of this leaflet carefully before you are given REVELLEX

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- 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.

1. WHAT REVELLEX CONTAINS

The active substance is infliximab.

The other ingredients are polysorbate, sodium phosphate and sucrose.

2. WHAT REVELLEX IS USED FOR

REVELLEX is intended for the treatment of rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, Crohn's disease and ulcerative colitis, with the aim to reduce inflammatory activity.

The active substance infliximab, is a human-mouse monoclonal antibody. Monoclonal antibodies are proteins that recognise and bind to other unique proteins in the body.

Infliximab ties up a special protein in the body called called tumour necrosis factor alpha (TNFα), which is involved in inflammation. Increased amounts of TNFα are common in inflammatory diseases such as rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, Crohn's disease and ulcerative colitis.

3. BEFORE YOU ARE GIVEN REVELLEX

You should not be administered REVELLEX

- if you are hypersensitive (allergic) to infliximab or to any of the other ingredients of REVELLEX.
- 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.

Take special care with REVELLEX

- **Hypersensitivity:** Some patients had an allergic reaction within 2 hours of receiving REVELLEX. These reactions were generally mild to moderate; however, on rare occasions they were severe. The symptoms of such reactions were most often skin rash, hives, fatigue, wheezing, difficulty in breathing and/or low blood pressure. If you notice any of these symptoms, tell your doctor.

  If the symptoms occur during your infusion, your doctor may slow down the speed of the infusion. Your doctor may also stop giving REVELLEX until the symptoms go away and then begin giving REVELLEX again. Your doctor may also treat your symptoms with other medicines (paracetamol, antihistamines, corticosteroids, bronchodilators and/or adrenaline). Most of the time, you can still receive REVELLEX even if the symptoms occur. However, in some cases your doctor may decide that it is best not to give you REVELLEX anymore.

  There is an increased risk of hypersensitivity reactions if you are retreated after an interval of more than 16 weeks. Therefore, taking REVELLEX again after an REVELLEX-free period of more than 16 weeks is not recommended.

  An allergic reaction may occur up to 12 days after your infusion. This reaction can be serious. Signs and symptoms are tenderness or pain in the muscles, rash, fever, joint or jaw pain, hand and face swelling, swallowing difficulties, itching, sore throat and/or headache. If you notice any of these symptoms, tell your doctor immediately.

- **Infections:** You might get infections more easily. It is important that you tell your doctor if you get any symptoms of infection e.g. fever, feeling generally unwell, wounds or dental problems. Before receiving treatment with REVELLEX you should tell your doctor if you have lived in or travelled to an area where infections called tuberculosis, histoplasmosis, coccidiomycosis or blastomycosis are common. These infections are caused by specific types of bacteria and fungi that can affect the lungs or other parts of your body. If you have fistulas that are leaking pus, please inform your doctor.

Tuberculosis (TB): Your doctor will test you to see if you have tuberculosis. 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. If your doctor feels that you are at risk for tuberculosis, you may be treated with medicines for tuberculosis before you begin REVELLEX therapy. If symptoms of tuberculosis (such as persistent cough, weight loss, tiredness, fever), or any other infection appear during therapy notify your doctor immediately.

- **Hepatitis B Virus:** 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. In some rare cases, especially if you are taking other medicines that suppress the immune system, reactivation of the hepatitis B virus can be life-threatening.

- **Cancer/Lymphoma:** Before you use REVELLEX, tell your doctor if you have had lymphoma (a type of blood cancer) or any other cancer. If you use REVELLEX, your risk for developing lymphoma or another cancer may increase. You should also tell your doctor if you develop lymphoma or other cancers while you are taking REVELLEX.

Reports of lymphoma in patients on REVELLEX are rare but occur more often than expected for people in general. A patient with more serious rheumatoid arthritis who has had the disease for a long time may be more prone to develop lymphoma.

Cancers, other than lymphoma, have also been reported in patients with a specific type of lung disease called Chronic Obstructive Pulmonary Disease (COPD). Patients with COPD and/or patients who are heavy smokers may be at increased risk for cancer with REVELLEX treatment. If you have COPD or are a heavy smoker you should discuss with your doctor whether REVELLEX is appropriate for you.

- **Heart failure:** If you have heart failure and you are being treated with REVELLEX, 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.

- **Neurological disease:** In rare instances patients treated with TNF blockers may develop diseases such as multiple sclerosis. Tell your doctor if you have a history of a neurological disease. If you develop symptoms of neurological disease such as changes in your vision, weakness in your arms or legs, numbness or tingling in any part of your body, you should contact your doctor right away.

- **Vaccinations:** You should not receive certain vaccines while using REVELLEX. If you have recently received or are scheduled to receive a vaccine, please inform your doctor.

- On rare occasions, you may develop signs and symptoms of a disease called lupus (persistent rash, fever, joint pain and tiredness). If these symptoms occur, contact your doctor.

- **Special patient groups:** REVELLEX is not recommended for use in children 17 years old or younger, except in Crohn's and ulcerative colitis diseases. REVELLEX has not been studied in children with Crohn's disease below the age of 6 years. Specific studies with REVELLEX have not been done in elderly patients, or in patients with hepatic or renal disease.

Receiving REVELLEX with food and drink

REVELLEX can be used with or without food or drink.

Pregnancy and breastfeeding

The effects of REVELLEX in pregnant women are not known so the use of REVELLEX in pregnant women is not recommended. If you are being treated with REVELLEX, you must avoid getting pregnant by using adequate contraception during your treatment and for at least 6 months after the last REVELLEX infusion.

It is not known whether REVELLEX is excreted in breast milk. If you are a breastfeeding mother or would like to start breastfeeding, you should discuss with your doctor whether treatment with REVELLEX is appropriate for you.

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before receiving REVELLEX.

Driving and using machines

It is not expected that REVELLEX will affect your ability to drive or use machines.

Using other medicines with REVELLEX

Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines).

- Generally, patients who have rheumatoid arthritis, Crohn's disease, ulcerative colitis, ankylosing spondylitis, psoriatic arthritis or psoriasis, already take several medicines, such as methotrexate, azathioprine or 6-mercaptopurine to treat their disease. These medicines may themselves cause side effects.
- Tell your doctor or pharmacist if you are taking anakinra because it should not be taken together. Also tell your doctor or pharmacist if you are taking any other medicines that affect your immune system.

4. HOW TO USE REVELLEX

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

Always use REVELLEX exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

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

REVELLEX is supplied as a powder for concentration for solution for infusion. This means that before REVELLEX is given to you, it is first dissolved in water for injections. The resulting solution is then further diluted with sodium chloride 0, 9 % solution for infusion.

REVELLEX is given to you in a vein, usually in your arm, over a 2-hour period in a healthcare facility. Your doctor or assistant will be monitoring you while you receive your REVELLEX dose and 1 to 2 hours thereafter. After the third treatment, your doctor may decide to give your REVELLEX over a 1 hour period.

Depending on your disease and if you respond, your doctor will decide on your individual dose and dosing interval. This may include additional doses at 2 to 6 weeks after your first dose. Treatment may also be continued thereafter. The total amount of REVELLEX given to you is based on the dose and your body weight. Your doctor will advise you what other medicines you must continue to take while on REVELLEX.

Rheumatoid arthritis: The recommended starting dose is 3 mg for every kg of body weight.

Ankylosing spondylitis: The recommended dose is 5 mg for every kg of body weight.

Psoriatic arthritis: The recommended dose is 5 mg for every kg of body weight.

Psoriasis: The recommended dose is 5 mg for every kg of body weight.

Crohn's disease: The recommended dose for severe, active Crohn's disease is 5 mg for every kg of body weight. The recommended dose for closure of enterocutaneous fistulas is 5 mg for every kg of body weight.

Ulcerative colitis: The recommended dose is 5 mg for every kg of body weight.

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

5. POSSIBLE SIDE EFFECTS

REVELLEX can have side effects. Side effects may appear up to 6 months after the last infusion.

Tell your doctor immediately if you notice any of the following:

- pain or tenderness in chest, muscles, joints or jaw
- swelling of the hands, feet, ankles, face, lips, mouth or throat which may cause difficulty in swallowing or breathing
- hives or other signs of an allergic reaction
- fever
- rash
- itching
- shortness of breath with exertion or upon lying down or swelling of the feet.

Tell your doctor as soon as possible if you notice any of the following:

- signs of infection
- difficulty breathing and non-productive cough
- problems with urination
- changes in the way your heart beats e.g. if you notice it beating faster
- light-headedness
- tiredness
- hoarseness
- coughing

- headache
- signs of neurological problems: seizures, tingling or numbness in any part of your body, weakness in arms and/or legs, eye problems, changes in vision
- signs of liver or spleen problems: eyes or skin turning yellow, dark-brown coloured urine, upper abdominal pain
- loss of weight
- night sweating.

The symptoms described above can be signs of the side effects listed below, which have been observed with REVELLEX.

Frequent side effects (likely to occur in less than 1 in 10 patients): headache, dizziness, nausea, abdominal symptoms, allergic reactions, rash, urticaria, viral infections (e.g. influenza, herpes), respiratory infections (cold, sinus infections, bronchitis, pneumonia).

Less frequent side effects (likely to occur in less than 1 in 100 patients): depression, agitation, sleep disturbances, impaired wound healing, bacterial infections (e.g. tuberculosis, urinary tract infections, deep skin infections, sepsis), fungal infections, asthma, abnormal liver function, low blood cell counts including anaemia, worsening of demyelinating nerve disease, autoimmune disease activation (lupus), worsening of heart failure, hair loss, bleeding, allergic anaphylactic reactions, injection site reactions.

Rare side effects (likely to occur in less than 1 in 1 000 patients): gastrointestinal bleedings or perforation, circulatory failure, multiple sclerosis, lymphoma.

Your doctor may also do tests to examine your liver function and/or blood values.

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 doctor, pharmacist or other healthcare professional for advice.

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

6. STORING AND DISPOSING OF REVELLEX

Store all medicines out of reach 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.

7. PRESENTATION OF REVELLEX

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

8. IDENTIFICATION OF REVELLEX

White solid with no evidence of meltback, free from foreign particles.

9. REGISTRATION NUMBER

33/30.1/0531

10. NAME AND BUSINESS ADDRESS OF THE REGISTRATION HOLDER

JANSSEN PHARMACEUTICA (PTY) LTD

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11. DATE OF PUBLICATION

- the date on the registration certificate of the medicine: 20 October 2000.
- the date of the most recently revised patient information leaflet as approved by Medicine Control Council: 12 May 2016