Patient Information Leaflet

SCHEDULING STATUS: S4

NPLATE 250 µg (Powder for solution for injection)

NPLATE 500 µg (Powder for solution for injection)

Romiplostim

Read all of this leaflet carefully before you start using NPLATE

- 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.

What is in this leaflet

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

1. What NPLATE is and what it is used for

NPLATE's active ingredient is romiplostim, which is a protein used to treat low platelet counts in patients with immune (idiopathic) thrombocytopenic purpura (called ITP). ITP is a disease in which your body's immune system destroys its own platelets. Platelets are the cells in your blood that help seal cuts and form blood clots. Very low platelet counts can cause bruising and serious bleeding.

NPLATE is used to treat adult patients with ITP who may or may not have had their spleen removed and who have been previously treated with

corticosteroids or immunoglobulins, where these treatments don't work.

NPLATE is also used to treat patients aged 1 year and over who may or may not have had their spleen removed for chronic ITP and who have been previously treated with corticosteroids or immunoglobulins, where these treatments don't work.

NPLATE works by stimulating the bone marrow (part of the bone which makes blood cells) to produce more platelets. This should help to prevent bruising and bleeding associated with ITP.

2. What you need to know before you use NPLATE

Do not use NPLATE:

- If you are allergic (hypersensitive) to romiplostim or to any of the other ingredients of NPLATE.
- If you are allergic to other biologic-prepared medicines that are produced by DNA technology using the micro-organism Escherichia coli (E. coli).

Tell your doctor if any of these apply, before you are given the injection.

Warnings and precautions

- If you stop taking NPLATE a low blood platelet count (thrombocytopenia) is likely to reoccur. If you stop taking NPLATE your platelet count will have to be monitored, and your doctor will discuss appropriate precautions with you.
- If you are at risk of blood clots or if blood clots are common in your family. The risk of blood clotting may also be increased if you:
  - have liver problems;
  - are elderly;
  - are bedridden;
  - have cancer;
  - are taking the contraceptive pill or hormone replacement therapy;

- have recently had surgery or suffered an injury;
- are obese (overweight);
- are a smoker.

Please tell your doctor if any of these apply to you before taking NPLATE.

- If you have very high blood platelet counts, this may increase the risk of blood clotting.

  Your doctor will adjust your dose of NPLATE to ensure that your platelet count does not become too high.

<u>Bone marrow changes (increased reticulin and possible bone marrow fibrosis)</u>

Long-term use of NPLATE may cause changes in your bone marrow. These changes may lead to abnormal blood cells or your body making less blood cells. The mild form of these bone marrow changes is called “increased reticulin” and has been observed in NPLATE clinical trials. It is not known if this may progress to a more severe form called “fibrosis.” Signs of bone marrow changes may show up as abnormalities in your blood tests. Your doctor will decide if abnormal blood tests mean that you should have bone marrow tests or if you should stop taking NPLATE.

<u>Worsening of blood cancers</u>

NPLATE is not for use in patients with blood cancer or a precancerous condition called myelodysplastic syndrome (MDS). If you have one of these conditions, there is a theoretical risk that NPLATE may worsen your cancer or condition.

<u>Loss of response to NPLATE</u>

If you experience a loss of response or failure to maintain a platelet response with romiplostim treatment, your doctor will investigate the reasons why including whether you are experiencing increased bone marrow fibres (reticulin) or have developed antibodies which neutralise romiplostim’s activity.

Children and Adolescents

NPLATE is not recommended for use in children aged under 1 year.

Other Medicines and NPLATE

Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines). If you are also taking medicines which prevent blood clots (anticoagulants or antiplatelet therapy) there is a greater risk of bleeding. Your doctor will discuss this with you.

If you are taking corticosteroids, danazol, and/or azathioprine (which you may be receiving to treat your ITP), these may be reduced or stopped when given together with NPLATE.

If you are taking or have recently taken any other medicines on a regular basis, including complementary or traditional medicines, the use of NPLATE with these medicines may cause undesirable interactions.
Please consult your doctor, pharmacist or other healthcare professional, for advice.

NPLATE with food and drink

There are no known specific food or drink restrictions when on NPLATE.

Pregnancy and breastfeeding

It is important to tell your doctor if you are pregnant; think you may be pregnant; or plan to get pregnant. NPLATE is not recommended for use if you are pregnant.

It is not known whether romiplostim is present in human milk. NPLATE is not recommended for use if you are breastfeeding.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

You should speak with your doctor before driving or using machines, as some side effects (e.g. temporary bouts of dizziness) may impair your ability to do so safely.

NPLATE contains sucrose and mannitol

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

NPLATE contains mannitol and may have a laxative effect.

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

3. How to use NPLATE

Adult and children (1 to 17 years):
NPLATE will be given under the direct supervision of your doctor, who will closely control the amount of NPLATE given to you.

NPLATE is administered once a week as an injection under the skin (subcutaneous).

Your doctor will tell you how much NPLATE will be given to you. NPLATE should be injected once per week in order to keep your platelet counts up. Your doctor will take regular blood samples to measure how your platelets are responding and may adjust your dose as necessary.

Once your platelet count is under control, your doctor will continue to regularly check your blood. Your dose may be adjusted further in order to maintain long-term

control of your platelet count.

Children (1 to 17 years old): in addition to adjusting your dose based on platelet counts, your doctor will also regularly reassess your body weight in order to adjust your dose.

If you take more NPLATE than you should

Your doctor will ensure that you receive the right amount of NPLATE.

If you have been given more NPLATE than you should, you may not experience any physical symptoms but your blood platelet counts may rise to very high levels and this may increase the risk of blood clotting. Therefore, if your doctor suspects that you have been given more NPLATE than you should, it is recommended that you are monitored for any signs or symptoms of side effects and that you are given appropriate treatment immediately.

If you forget to use NPLATE

Your doctor will discuss with you when you should have your next dose.

If you stop using NPLATE

If you stop using NPLATE, your low blood platelet count (thrombocytopenia) is likely to reoccur.

Your doctor will decide if you should stop using NPLATE.

4. Possible Side Effects

NPLATE can have side effects.

Not all side effects reported for NPLATE are included in this leaflet.

Should your general health worsen or if you experience any untoward effects while taking this medicine, please consult your doctor, pharmacist or other healthcare

professional for advice.

If any of the following happen, stop taking NPLATE and tell your doctor immediately or go to the casualty department at your nearest hospital:

- allergic reaction (hypersensitivity); injection site reactions; redness of the skin (flushing);
- Severe allergic reaction (anaphylactic reaction); swelling of the face (face oedema), lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing (angioedema) (dyspnoea).
- swelling of the hands, feet and ankles
- allergic reaction in the skin upon contact with allergen (contact dermatitis); skin manifestation with rash and blisters (eczema); dry skin; redness of the skin (erythema);severe flaking or peeling rash (exfoliative rash); abnormal hair growth; thickening and itching of the skin due to repeated scratching (prurigo); bleeding beneath the surface of the skin or bruising under the skin purpura); bruising (contusion); bumpy skin rash (papular rash); itchy skin rash (pruritic rash); generalised itchy rash (urticaria); bump on the skin (skin nodule);
- higher than normal platelet counts (thrombocytosis);
- blood clot in a lung artery (pulmonary embolism);
- blood clot in the transverse sinus (transverse sinus thrombosis); problems with the circulation including blood clot in the vein in the liver (portal vein thrombosis); deep vein thrombosis; blocking of a blood vessel or (peripheral embolism); reduced blood flow in the hands, ankles or feet (peripheral ischaemia); swelling and clotting in a vein, which may be extremely tender when touched (phlebitis or superficial thrombophlebitis); blood clot (thrombosis).
- low blood platelet count (thrombocytopenia) and low blood platelet count (thrombocytopenia) after stopping NPLATE; bleeding of the vagina (vaginal

haemorrhage), bleeding in the mouth (mouth haemorrhage); bleeding in the eye (conjunctival haemorrhage); injection site bleeding (injection site haemorrhage);

- bone marrow disorder that causes scarring (myelofibrosis); including increased bone marrow fibres (reticulin);
- a rare type of anaemia in which the red blood cells, white blood cells and platelets are all reduced in number (aplastic anaemia);
- raised white blood cell count (leucocytosis);
- cancer of white blood cells (multiple myeloma);
- enlarged spleen (splenomegaly);
- blindness.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to NPLATE. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- heart attack (myocardial infarction); increased heart rate;
- palpitations; chest pain; redness of the skin (flushing);
- problems with your nervous system including involuntary
- muscle contractions (clonus);
- dehydration;
- protein in the urine.
- changes in some blood tests (increase in transaminase; increased blood lactate dehydrogenase);
- fever (pyrexia); chills; flu-like symptoms (influenza-like illness);
- influenza; localised infection; inflammation of the sinuses (sinusitis); inflammation of the passages in the nose and throat (nasopharyngitis); inflammation of the passages that carry air to the lungs (bronchitis);

problems with the nose and throat including: cough; runny nose (rhinitis); sinusitis dry throat; nasal congestion; painful breathing (painful respiration); pain in the nose and throat (oropharyngeal pain); sore throat and discomfort when swallowing (pharyngitis);

- itchy eye (eye pruritus); inflammation of the eye (conjunctivitis);
- ear infection;
- upper respiratory tract infection
- gastroenteritis
- painful swollen joints caused by uric acid (food breakdown product) (gout);

These are all very serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

- headache;
- migraine;
- trouble sleeping (insomnia);
- depression; abnormal dreams;
- dizziness or a spinning sensation (vertigo);
- difficulty focussing or blurred vision (accommodation disorder, papilloedema or eye disorder); increased tears (increased lacrimation); or visual disturbances; sensitivity to light (photosensitivity reaction);
- distorted sense of taste (dysgeusia); decrease in sense of taste (hypogeusia); bad breath (breath odour); difficulty swallowing (dysphagia); mouth ulcers or mouth blistering (stomatitis); discoloured teeth (tooth discolouration);
- upper abdominal pain; stomach discomfort indigestion (dyspepsia); or heartburn (gastro-oesophageal reflux disease);
- vomiting
- nausea;
- diarrhoea;

- constipation;
- tiredness (fatigue);
- weakness (asthenia);
- pain;
- joint pain (arthralgia);
- bone pain;
- burning pain, redness and warmth in the feet and hands (erythromelalgia).
- muscle pain or weakness (myalgia);
- muscle spasm;
- decreased feeling of sensitivity, especially in the skin (hypoaesthesia); alteration in the nerve functions in the arms and legs (peripheral neuropathy); tingling or numbness of the hands or feet (paraesthesia);
- acne;
- hair loss (alopecia)
- alcohol intolerance

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

Not known: frequency cannot be estimated from the available data

- Severe allergic reaction (anaphylactic reaction) symptoms may include shortness of breath, flushing, itching, swelling of face and generalized swelling

Reporting of side effects

If you get side effects, talk to your doctor, 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 NPLATE.

Alternatively, you can report side effects to:

Amgen South Africa (Pty) Ltd.

Tel: +27 (0)11 100 5300

Email: safety-south-africa@amgen.com

5. How to store NPLATE

Store all medicines out of reach of children.

Do not use NPLATE after the expiry date which is stated on the carton and vial label after EXP.

The expiry date refers to the last day of that month.

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

Do not freeze.

Store in the original carton in order to protect from light.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What NPLATE contains

The active substance is romiplostim.

Each vial of NPLATE 250 µg powder for solution for injection contains a total of 375 µg of romiplostim. An additional overfill is included in each vial to ensure that 250 µg of romiplostim can be delivered. After reconstitution, a deliverable volume of 0,5 ml solution contains 250 µg of romiplostim(500 µg/ml).

Each vial of NPLATE 500 µg powder for solution for injection contains a total of 625 µg of romiplostim. An additional overfill is included in each vial to ensure

that 500 µg of romiplostim can be delivered. After reconstitution, dissolving, a deliverable amount of 1,0 ml solution contains 500 µg of romiplostim (500 µg /ml).

Contains sugar [mannitol (E421) and sucrose].

The other ingredients are dilute hydrochloric acid (for pH adjustment), L-histidine and polysorbate 20.

What NPLATE looks like and contents of the pack

NPLATE is a white powder in a clear 5 ml glass vial with a grey stopper, aluminium seal and either a red (250 µg) or blue (500 µg) flip-off cap.

NPLATE is a solution for injection supplied in a single-dose 5 ml glass vial in a carton.

A carton will contain 1 or 4 vials of either 250 µg or 500 µg of romiplostim.

Not all pack sizes may be marketed.

Holder of Certificate of Registration

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2021

This leaflet was last revised in

Date of Registration: 07 December 2012

Updated: 04 March 2021

Registration number(s)

NPLATE 250 µg: 45/8.2/0175

NPLATE 500 µg: 45/8.2/0176