PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrNplate®

romiplostim for injection

Read this carefully before you start taking **NPLATE** 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 **NPLATE**.

Serious Warnings and Precautions

- NPLATE is not for use in patients, outside of a clinical research study, with blood cancer or a precancerous condition called myelodysplastic syndrome (MDS). If you have one of these conditions, NPLATE may worsen your cancer or condition and may cause you to die sooner.
- Despite ongoing treatment with NPLATE, serious bleeding could occur and patients should be closely monitored during treatment. Rescue medications including platelet transfusions might be required, especially for patients with unstable platelet counts.
- When you stop receiving NPLATE, your low blood platelet counts (thrombocytopenia) may become worse than before you started NPLATE. This may result in serious life-threatening or fatal bleeding.

What is NPLATE used for:

NPLATE is a protein used to treat low platelet counts in adult patients (aged 18 and over) with immune thrombocytopenia (called ITP). ITP is a disease in which the immune system of your body destroys your platelets. Platelets are the cells in your blood that help seal cuts and form blood clots. If you have too few platelets you could bruise easily and bleed for a long time after being injured. If your platelet count is very low, you may be at risk of serious, life-threatening bleeding events.

NPLATE is used in patients who have not had their spleen removed and are unable to tolerate corticosteroids and/or immunoglobulins or where these treatments have not worked. NPLATE is also used in patients who have had their spleen removed but the treatment has not worked.

How does NPLATE work?

Your doctor has given you NPLATE to stimulate your bone marrow (part of the bone which makes blood cells) to produce more platelets. This should help to prevent bruising and bleeding.

What are the ingredients in NPLATE?

Medicinal ingredients: romiplostim

Non-medicinal ingredients: diluted hydrochloric acid, L-histidine, mannitol (E421), polysorbate 20, and sucrose**.**

NPLATE comes in the following dosage forms:

NPLATE is a white powder for solution for injection, available in a vial.

Each pack contains 1 vial of either 625 micrograms or 375 micrograms of powder for solution for injection.

Do not use NPLATE if:

- you are allergic (hypersensitive) to romiplostim or any of the other ingredients of NPLATE.
- you are allergic to other products that are produced by DNA technology using the micro-organism *E. coli*.

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

- are taking or have recently taken any other medicines, including medicines obtained without a prescription
- have or have had any of the following medical conditions
  - liver problems
  - kidney problems
  - 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 (≥ 65 years), 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)
- are pregnant; think you may be pregnant; or plan to get pregnant. NPLATE has not been tested in pregnant women.

Care should be taken if you are breast-feeding, as it is not known whether NPLATE is present in human milk.

Treatment should be prescribed and monitored only by qualified healthcare providers.

NPLATE should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding.

NPLATE should not be used in an attempt to normalize platelet counts.

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.” It is not known if this may progress to a more severe form called “fibrosis.” The mild form may cause no problems while the severe form may cause life-threatening blood problems. Signs of bone marrow changes may show up as abnormalities in your blood tests. Your healthcare provider will decide if abnormal blood tests mean that you should have bone marrow tests or if you should stop taking NPLATE.

Your doctor may decide to take a bone marrow biopsy if they decide it is necessary to ensure that you have ITP, and not another condition such as Myelodysplastic Syndrome (MDS). If you have MDS and receive NPLATE, your MDS condition may worsen to become an acute myeloid leukemia, a type of cancer of the blood, which has been observed in adult clinical trials with NPLATE.

If your platelet counts have not improved after a few weeks of treatment with NPLATE, your doctor may decide to conduct more blood tests. It is also possible that your doctor may decide to stop your treatment because your bleeding condition has not improved.

Low blood platelet counts (thrombocytopenia) or bleeding events are likely to recur if you stop taking NPLATE. Your blood tests including platelet counts will have to be monitored, and your doctor will discuss appropriate precautions with you. Following discontinuation of NPLATE, thrombocytopenia and risk of bleeding may develop that is worse than that experienced prior to the NPLATE therapy.

Very high blood platelet counts may increase the risk of blood clotting. You may have severe complications or die from some forms of blood clots, such as clots that spread to the lungs or that cause heart attacks or strokes. If you have a chronic liver disease, you may get blood clots in the veins of your liver. This may affect your liver function. Your doctor will adjust your dose of NPLATE to ensure that your platelet count does not become too high.

Your doctor will determine the right amount of NPLATE that you should receive. 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. If you have been given less NPLATE than you should, you may not experience any physical symptoms but your blood platelet counts may become low and this may increase the risk of bleeding. Therefore if your doctor suspects that you have been given more or less 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.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

If you are also taking medicines that prevent blood clots (anticoagulants or anti-platelet therapy) there is a greater risk of bleeding. Your doctor will discuss this with you.

The following may interact with NPLATE:

- Drug interactions between NPLATE and other drugs have not been studied.

How to take NPLATE:

Treatment should be prescribed and monitored only by qualified healthcare providers.

NPLATE is administered as an injection under the skin (subcutaneous). Special care should be taken to ensure the appropriate volume of NPLATE is withdrawn from the vial.

Reconstitution of NPLATE:

NPLATE is a sterile but unpreserved product and is intended for single use only.

NPLATE should be prepared by carefully calculating the dose and reconstituting with the correct volume of sterile water for injection.

Each vial of NPLATE 250 micrograms powder for solution for injection contains a total of 375 micrograms of romiplostim. An additional overfill is included in each vial to ensure that 250 micrograms of romiplostim can be delivered. After reconstitution (dissolving) with 0.72 mL of sterile water for injection, a deliverable volume amount of 0.5 mL solution contains 250 micrograms of romiplostim (500 micrograms/mL).

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

micrograms of romiplostim can be delivered. After reconstitution (dissolving) with 1.2 mL of sterile water for injection, a deliverable volume amount of 1 mL solution contains 500 micrograms of romiplostim (500 micrograms/mL).

Do not use saline or bacteriostatic water when reconstituting the product. NPLATE should be reconstituted under aseptic conditions. The water for injection should be injected slowly into the NPLATE vial. The vial contents may be swirled gently and inverted during dissolution. Do not shake or vigorously agitate the vial. Generally, dissolution of NPLATE takes less than 2 minutes. Visually inspect the solution for particulate matter and discolouration before administration. Reconstituted NPLATE should be clear and colourless. NPLATE should not be administered if particulate matter and/or discolouration are observed.

The reconstituted product should be administered within 24 hours as it does not contain a preservative. The reconstituted product can remain at room temperature (25°C) or can be refrigerated at 2°C to 8°C for up to 24 hours prior to administration. The reconstituted product must be protected from light.

Any unused product or waste material should be disposed of in accordance with local requirements.

Initial dose:

Your initial dose is 1 microgram of NPLATE per kilogram of your body weight once a week.

Your doctor will tell you how much you must take. NPLATE is intended to 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.

Tell your healthcare provider about any bruising or bleeding that occurs while you are receiving NPLATE.

Overdose:

NPLATE is a highly potent drug, administered at a low volume dose. Therefore, there is a potential risk of incorrect volume being administered.

The sign of an NPLATE overdose may be an increase in platelet count, which may be higher than the normal range. Your healthcare provider may conduct additional blood tests to monitor your platelet count, and adjust your NPLATE dose.

If you think you, or a person you are caring for, have taken too much NPLATE, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you have missed a dose of NPLATE, your doctor will discuss with you when you should have your next dose.

What are possible side effects from using NPLATE?

Like all medicines, NPLATE can cause unwanted effects.

These are not all the possible side effects you may have when taking NPLATE. If you experience any side effects not listed here, tell your healthcare professional.

Very common (seen in more than 1 in 10 people taking NPLATE):

- aching joints (arthralgia)
- muscle aches (myalgia)
- pain in extremity
- dizziness
- difficulty sleeping (insomnia)

Common (seen in more than 1 in 100, but less than 1 in 10 people taking NPLATE):

- abdominal pain
- shoulder pain
- tingling or numbness of the hands or feet (paresthesia)
- upset stomach (dyspepsia)
- vomiting
- hypersensitivity
- inflammation of the sinuses (sinusitis)
- inflammation of the passages that carry air to the lungs (bronchitis)
- bleeding (hemorrhage)

Uncommon (seen in more than 1 in 1000, but less than 1 in 100 people taking NPLATE):

- redness, heat and pain of skin (erythromelalgia)

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.

Serious side effects and what to do about them			
Symptom / effect[a]	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
VERY COMMON			
Headache Headache may be a symptom of a blood clot.		√	
COMMON			
Low blood platelet count (thrombocytopenia) after stopping NPLATE When you stop treatment with NPLATE, your platelet count may drop to the level it was before you started treatment with NPLATE. The symptoms associated with your ITP condition that you had prior to treatment with NPLATE may recur, including bleeding. You should contact your doctor immediately if you stop taking NPLATE or if your symptoms recur.		√	
Higher than normal platelet counts (thrombocytosis) You may potentially experience symptoms indicative of a blood clot. Symptoms may include, but are not limited to, headache, tingling in hands or feet, swelling and possible redness in areas such as the calf. Contact your doctor immediately.		√	√
UNCOMMON			
Increased fibers (reticulin) in the bone marrow (bone marrow reticulin fibrosis) This finding can only be diagnosed by your doctor with special testing. Your doctor will determine whether to continue you on NPLATE or consider alternative treatment options.		√	
Angioedema You may potentially experience hive-like swelling beneath the skin. Contact your doctor immediately.		√	√

[a] Frequency reflects all adverse events (serious and non-serious)

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

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

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:

Store in a refrigerator at 2°C to 8°C (36°F to 46°F). Do not freeze.

Alternatively, unreconstituted vials of this medicine may be removed from the refrigerator for a period of up to 30 days in the original carton;

- If removed from the refrigerator, this medicine must be used within 30 days.
- If not used within the 30 days, discard NPLATE.

Store in original carton in order to protect from light and do not expose to temperatures above 25°C (77°F).

Do not use NPLATE after the expiry date which is stated on the carton and vial label. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required.

Keep out of reach and sight of children.

If you want more information about NPLATE:

- 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/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website (www.amgen.ca), or by calling 1-866-502-6436.

This leaflet was prepared by Amgen Canada Inc.

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