

The logo features the text "Nplate™ (romiplostim)" in a smaller font above the word "Nexus" in a larger, bold font. A gold-colored arc is positioned behind the text, starting from the left and curving over the top of "Nexus".

Nplate™ (romiplostim)
Nexus

Network of **EX**perts

Understanding and Supporting Nplate™ (romiplostim) and patients

The Nplate™ NEXUS Program connects you with Nplate™ access, support, education, and safety monitoring.

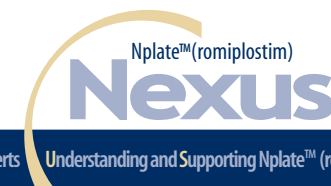
What is the Nplate™ (romiplostim) NEXUS Program?¹

Nplate™ is only available through the Nplate™ NEXUS (Network of EXperts Understanding and Supporting Nplate™ and patients) Program. This program is designed to promote informed risk-benefit decisions before initiating treatment and while patients are on treatment to assure appropriate use of Nplate™ for the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenic purpura (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Nplate™ should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increases the risk for bleeding. Nplate™ should not be used in attempt to normalize platelet counts. Nplate™ is not indicated for the treatment of thrombocytopenia due to MDS or any cause of thrombocytopenia other than chronic ITP.

The Nplate™ NEXUS Program consists of a patient registry and a requirement for prescribers to complete baseline and periodic safety information for every patient. As a prescriber, you must enroll in the Nplate™ NEXUS Program in order to prescribe Nplate™ by completing the Nplate™ NEXUS Program Healthcare Provider Enrollment Form. Prescribers are required to comply with the following program requirements:

- Read the full prescribing information for Nplate™.
- Understand the approved indication.
- Understand that Nplate™ should not be used in attempt to normalize platelet counts.
- Understand that Nplate™ is not indicated for the treatment of thrombocytopenia due to MDS or any cause of thrombocytopenia other than chronic ITP.
- Understand the risks associated with Nplate™.
- Understand that each patient should be monitored to assure safe use of Nplate™.
- Understand how to properly dose and administer Nplate™ in order to prevent medication errors.
- Understand that you must complete the Nplate™ NEXUS Program Healthcare Provider Enrollment Form to enroll in the Nplate™ NEXUS Program (only enroll once).

- Enroll each patient by completing the Nplate™ NEXUS Program Patient Enrollment Form and Nplate™ NEXUS Program Patient Baseline Data Form. Complete the Nplate™ NEXUS Program Patient Baseline Data Form at the time of enrollment or within 30 days of patient enrollment. Baseline data is only to be used to assess for risk factors for adverse events and to evaluate the long-term safety of Nplate™.
- Provide each patient with the Nplate™ Medication Guide prior to each dose and counsel each patient on the risks and benefits of Nplate™.
- Complete the Nplate™ NEXUS Program Patient Enrollment Form with each patient: (1) obtain patient's signature acknowledging receipt of Nplate™ Medication Guide, (2) obtain patient's signature authorizing disclosure of health information related to the Nplate™ NEXUS Program, and (3) send the completed Nplate™ NEXUS Program Patient Enrollment Form to the Nplate™ NEXUS Program for patient enrollment.
- Counsel each patient to carry a Patient ID Card and Dosing Tracker that identifies the risks with Nplate™ and contains the Nplate™ NEXUS Program access number.
- Evaluate the safe use and patient status every 6 months to determine whether the patient should continue Nplate™ and if so, authorize treatment for another 6 months.
- Notify the Nplate™ NEXUS Program when a patient discontinues Nplate™ by completing the Nplate™ NEXUS Program Patient Discontinuation/Post-Discontinuation Follow-up Form at the time of Nplate™ discontinuation and 6 months later.
- Promptly report to the Nplate™ NEXUS Program any adverse events occurring in the course of the use of the drug, as described in the Nplate™ NEXUS Program Safety Questionnaire.
- Understand that Amgen will be regularly evaluating compliance with the Nplate™ NEXUS Program, and that Amgen reserves the right to restrict a healthcare provider's ability to enroll future patients or take other appropriate measures at any time if a healthcare provider fails to comply with Nplate™ NEXUS Program requirements.



What risks are monitored through the Nplate™ NEXUS Program?¹

Bone marrow reticulin formation and risk for bone marrow fibrosis

- Nplate™ administration increases the risk for development or progression of reticulin fiber deposition within the bone marrow.
- In clinical studies, Nplate™ was discontinued in 4/271 patients because of bone marrow reticulin deposition. Six additional patients had reticulin observed upon bone marrow biopsy. All 10 patients with bone marrow reticulin deposition had received Nplate™ doses ≥ 5 mcg/kg, and six received doses ≥ 10 mcg/kg.
- Progression to marrow fibrosis with cytopenias was not reported in the controlled clinical studies. In the extension study, one patient with ITP and hemolytic anemia developed marrow fibrosis with collagen during Nplate™ therapy.
- Clinical studies have not excluded a risk of bone marrow fibrosis with cytopenias.
- Prior to initiation of Nplate™ examine the peripheral blood smear closely to establish a baseline level of cellular morphologic abnormalities. Following identification of a stable Nplate™ dose, examine peripheral blood smears and CBCs monthly for new or worsening morphological abnormalities (eg, teardrop and nucleated red blood cells, immature white blood cells) or cytopenia(s).
- If the patient develops new or worsening morphological abnormalities or cytopenia(s), discontinue treatment with Nplate™ and consider a bone marrow biopsy, including staining for fibrosis.

Worsened thrombocytopenia after cessation of Nplate™

- Discontinuation of Nplate™ may result in thrombocytopenia of greater severity than was present prior to Nplate™ therapy. This worsened thrombocytopenia may increase the patient's risk of bleeding, particularly if Nplate™ is discontinued while the patient is on anticoagulants or antiplatelet agents.
- In clinical studies of patients with chronic ITP who had Nplate™ discontinued, 4/57 patients developed thrombocytopenia of greater severity than was present prior to Nplate™ therapy.
- This worsened thrombocytopenia resolved within 14 days.
- Following discontinuation of Nplate™, obtain weekly CBCs, including platelet counts, for at least 2 weeks and consider alternative treatments for worsening thrombocytopenia, according to current treatment guidelines.

Thrombotic/thromboembolic complications

- Thrombotic/thromboembolic complications may result from excessive increases in platelet counts. Excessive doses of Nplate™ or medication errors that result in excessive Nplate™ doses may increase platelet counts to a level that produces thrombotic/thromboembolic complications. In controlled clinical studies, the incidence of thrombotic/thromboembolic complications was similar between Nplate™ and placebo.
- To minimize the risk for thrombotic/thromboembolic complications, do not use Nplate™ in an attempt to normalize platelet counts. Follow the dose adjustment guidelines to achieve and maintain a platelet count $\geq 50 \times 10^9/L$.

Hematological malignancies and progression of malignancy in patients with a pre-existing hematological malignancy or myelodysplastic syndrome (MDS)

- Nplate™ stimulation of the TPO receptor on the surface of hematopoietic cells may increase the risk for hematologic malignancies. In controlled clinical studies among patients with chronic ITP, the incidence of hematologic malignancy was low and similar between Nplate™ and placebo.
- In a separate single-arm clinical study of 44 patients with myelodysplastic syndrome (MDS), 11 patients were reported as having possible disease progression, among whom four patients had confirmation of acute myelogenous leukemia (AML) during follow-up.
- Nplate™ is not indicated for the treatment of thrombocytopenia due to MDS or any cause of thrombocytopenia other than chronic ITP.

Non-ITP populations

- Nplate™ is not indicated for the treatment of thrombocytopenia due to MDS or any cause of thrombocytopenia other than chronic ITP.

Medication error due to small volumes administered

- Medication errors may occur because Nplate™ is administered in small volumes, and small differences in dose can have large effects on platelet counts. Healthcare providers should pay special attention to accurate calculation of the dose of Nplate™, transcription of the medication order, and dosing instructions to minimize the risk of medication errors, overdose, and underdose.
- Nplate™ must be administered by the enrolled prescribers or healthcare providers under their direction.



How do I enroll in the Nplate™ NEXUS Program?¹

Enrollment is simple:

1. Read and understand the Nplate™ package insert and the requirements of the Nplate™ NEXUS Program.
2. Review, complete, and submit the Nplate™ NEXUS Program Healthcare Provider Enrollment Form. Provider enrollment is completed only once.
3. Identify an appropriate patient for Nplate™, educate the patient on the risks and benefits of treatment with Nplate™, make sure that the patient receives the Medication Guide, instruct the patient to read it, and encourage the patient to ask questions when considering Nplate™.
4. Review, complete, and submit the Nplate™ NEXUS Program Patient Enrollment Form, answer all questions, and obtain the patient's signature on the Nplate™ NEXUS Program Patient Enrollment Form. Keep the original, send a copy according to Nplate™ NEXUS Program instructions, and give a copy to the patient.
5. Complete and submit the Nplate™ NEXUS Program Patient Baseline Data Form.

Fax completed forms to 1-877-NPLATE0 (1-877-675-2830) using the forms provided in your Nplate™ NEXUS Program Training Kit, or go online at www.nplate.com to download the forms

The diagram on the next page lays out the steps of the Nplate™ NEXUS Program. Anytime a healthcare provider or patient has a question about Nplate™ use, risks, ITP reimbursement, or other support services, they can call the Nplate™ NEXUS Program at 1-877-NPLATE1 (1-877-675-2831), and a NEXUS Specialist will assist them.

Connecting with Nplate™ (romiplostim) therapy: The five steps of the Nplate™ NEXUS Program

Healthcare Provider Enrollment

- Read and understand the Nplate™ package insert and the requirements of the Nplate™ NEXUS Program.
- Review, complete, and submit the Nplate™ NEXUS Program Healthcare Provider Enrollment Form. Provider enrollment is completed only once.
 - If desired, you may also order a small safety stock for emergency only. This safety stock can be ordered only by calling 1-877-NPLATE1 (1-877-675-2831).

Patient Enrollment

- Identify an appropriate patient for Nplate™, educate the patient on the risks and benefits of treatment with Nplate™, make sure that the patient receives the Medication Guide, instruct the patient to read it, and encourage the patient to ask questions when considering Nplate™.
- Review, complete, and submit the Nplate™ NEXUS Program Patient Enrollment Form, answer all questions, and obtain the patient's signature on the Nplate™ NEXUS Program Patient Enrollment Form. Keep the original, send a copy according to Nplate™ NEXUS Program instructions, and give a copy to the patient.
 - Complete and submit the Nplate™ NEXUS Program Patient Baseline Data Form.

ITP Reimbursement Assistance (optional)

- Upon enrollment, complete an ITP reimbursement assistance form, if desired.
 - NEXUS Specialists can answer questions about Nplate™ and ITP reimbursement at 1-877-NPLATE1 (1-877-675-2831).

Fulfillment

- Nplate™ can be ordered through your normal distributor or directly through the Nplate™ NEXUS Program.
- Healthcare providers should only order enough Nplate™ to meet the immediate needs of individual enrolled patients.
 - The NEXUS Specialist confirms that you are enrolled in the program and are treating enrolled patients.
 - A NEXUS Specialist arranges shipment of Nplate™ to your office. Shipments will usually be received within 48 hours.

Support and Follow-up

- Twice a year, a NEXUS Specialist will contact you to verify the enrolled patient roster, collect safety information, and verify whether each patient should continue on Nplate™.

Nplate™ (romiplostim)
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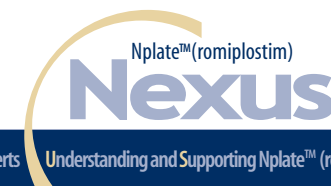
1-877-NPLATE1 (1-877-675-2831)

How do I order Nplate™?

- Once you and your patient are enrolled in the Nplate™ NEXUS Program, place an order with your preferred distributor, or call 1-877-NPLATE1 (1-877-675-2831), and a NEXUS Specialist will facilitate your order through your normal distributor.
- The NEXUS Specialist confirms that you are enrolled in the program and are treating enrolled patients.
- Your order will be forwarded to the Nplate™ NEXUS Program, where a NEXUS Specialist will call your office to arrange shipment.
- If desired, you may also order a small safety stock for emergency only. This safety stock can be ordered only by calling 1-877-NPLATE1 (1-877-675-2831).
- Nplate™ usually ships within 48 hours in an insulated cold-shipping container to your office.

What do I do for the Nplate™ NEXUS Program during Nplate™ treatment?

- Order Nplate™ for your patients through your primary wholesaler or call 1-877-NPLATE1 (1-877-675-2831). Healthcare providers should only order enough Nplate™ to meet the immediate needs of individual enrolled patients.
- Provide each patient with the Medication Guide prior to each Nplate™ injection.
- Promptly report any adverse events associated with the use of Nplate™ to the Nplate™ NEXUS Program at 1-877-675-2831 or FDA's MedWatch Program at 1-800-FDA-1088.
- Twice a year, verify your patient roster, then complete and submit an Nplate™ NEXUS Program Safety Questionnaire for each patient by fax (1-877-NPLATE0 [1-877-675-2830]), or phone (1-877-NPLATE1 [1-877-675-2831]). You will verify that each patient should continue on Nplate™.
- For any report of a serious adverse event, Amgen will follow up for more information. You can provide more detailed information by submitting the MedWatch form by fax (1-877-NPLATE0 [1-877-675-2830]), or giving the information over the phone (1-877-NPLATE1 [1-877-675-2831]).



What do I do if a patient discontinues Nplate™ treatment?

- Complete and submit the Nplate™ NEXUS Program Patient Discontinuation/Post-Discontinuation Follow-up Form at time of discontinuation and 6 months later. The form can be submitted by fax (1-877-NPLATE0 [1-877-675-2830]), or phone (1-877-NPLATE1 [1-877-675-2831]).
- Call 1-877-NPLATE1 (1-877-675-2831) to inquire about product returns.

What ITP reimbursement support is available?

The Nplate™ NEXUS Program will provide optional ITP reimbursement assistance to patients and healthcare providers.

ITP reimbursement services include:

- Verifying insurance coverage
- Assisting with alternative funding options
- Assistance with prior authorizations, claims, denials, and appeals

What other risks are associated with Nplate™?¹

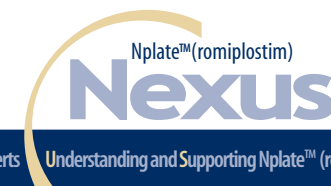
Lack or loss of response to Nplate™

- Hyporesponsiveness or failure to maintain a platelet response with Nplate™ should prompt a search for causative factors, including neutralizing antibodies to Nplate™ or bone marrow fibrosis.
- To detect antibody formation, submit blood samples to Amgen at 1-800-772-6436. Amgen will assay these samples for antibodies to Nplate™ and thrombopoietin (TPO).
- Discontinue Nplate™ if the platelet count does not increase to a level sufficient to avoid clinically important bleeding after 4 weeks at the highest weekly dose of 10 mcg/kg.

Common adverse drug reactions

- In the placebo-controlled studies, headache was the most commonly reported adverse drug reaction, occurring in 35% of patients receiving Nplate™ and 32% of patients receiving placebo. Headaches were usually of mild or moderate severity.
- Most common adverse reactions ($\geq 5\%$ higher patient incidence in Nplate™ versus placebo) were Arthralgia (26%, 20%), Dizziness (17%, 0%), Insomnia (16%, 7%), Myalgia (14%, 2%), Pain in Extremity (13%, 5%), Abdominal Pain (11%, 0%), Shoulder Pain (8%, 0%), Dyspepsia (7%, 0%), and Paresthesia (6%, 0%).

See the following pages for hospital and institutional enrollment.



For institutional enrollment only (not for individual practices)

Hospital and Institutional Enrollment

The Nplate™ NEXUS Program offers the flexibility of institutional enrollment

Hospitals and other healthcare institutions may enroll by submitting an Nplate™ NEXUS Program Institution Enrollment Form. Upon enrollment, an institution may designate an Nplate™ NEXUS Program point of contact for the institution. The designated person may be a hospital administrator, pharmacy director, clinical pharmacist, or any staff member the institution deems appropriate to internally coordinate Nplate™ NEXUS Program activities.

During enrollment, the designated person will complete an Nplate™ NEXUS Program Institution Enrollment Form agreeing to the following:

- Develop a system, order sets, protocols, or other measures to ensure that Nplate™ is only dispensed to inpatients and outpatients (eg, in a clinic) after verifying that the prescribing healthcare provider and patient are enrolled in the Nplate™ NEXUS Program;
- Train and provide educational materials to appropriate staff responsible for prescribing, dispensing, and administering Nplate™ regarding the safe and appropriate use of Nplate™, program monitoring requirements (including dispensing a Medication Guide with each dose), program adverse event reporting requirements, and institution documentation requirements;
- Develop a system to ensure patients started on Nplate™ as inpatients are transitioned to an outpatient healthcare provider that is enrolled (or will be enrolled) in the Nplate™ NEXUS Program; and
- Develop a process and system to track Nplate™ NEXUS Program compliance and cooperate with periodic audits to assure that Nplate™ is used in accordance with the program requirements.

Product tracking includes the following information:

- Name and unique identification number of the enrolled prescribing healthcare provider
- Unique identifier (program ID number, name, date of birth, address) of the enrolled patient receiving Nplate™
- Date of each Nplate™ order (including number of vials ordered and vial sizes)
- Number of Nplate™ vials, vial sizes, and date of each dose given to each patient
- Overall inventory for the set period of time including the total number of vials ordered, dispensed, and in stock

The designated contact will receive the Nplate™ NEXUS Program Training Kits for in-house training along with copies of the Nplate™ Medication Guide. NEXUS Specialists and Amgen representatives will be available as resources to institutions and assist healthcare providers in the enrollment and training. Please note: In addition to institutional enrollment, all individual healthcare providers must be enrolled in the Nplate™ NEXUS Program in order to prescribe Nplate™.

Amgen will be regularly evaluating program compliance to ensure that program objectives are met. Amgen reserves the right to terminate an institution enrollment at any time based upon the institution's noncompliance with program requirements, or take other appropriate measures to assure that program objectives are met.

Ordering Nplate™

Once an institution and patient(s) are enrolled, an institution will receive an enrollment confirmation. This enrollment must be completed only once. Ordering and billing for Nplate™ will occur through your primary wholesaler. A NEXUS Specialist will arrange shipment directly to the institution.

If desired, you may also order a small safety stock for emergency only. This safety stock can be ordered only by calling 1-877-NPLATE1 (1-877-675-2831).

Prescribing Nplate™

When a healthcare provider enrolled in the Nplate™ NEXUS Program identifies and prescribes Nplate™ to an appropriate patient, a designated hospital staff member will check with the Nplate™ NEXUS Program to verify that the patient was previously enrolled in the program. An Nplate™ NEXUS Program Patient Enrollment Form must be completed for any new patient.

Record-keeping

Enrolled institutions will be required to maintain drug accountability and reconciliation records. This may include, at minimum, the following information:

- Name and unique identification number of the enrolled prescribing healthcare provider
- Unique identifier (program ID number, name, date of birth, address) of the enrolled patient receiving Nplate™
- Date of each Nplate™ order (including number of vials ordered and vial sizes)
- Number of Nplate™ vials, vial sizes, and date of each dose given to each patient
- Overall inventory for the set period of time including the total number of vials ordered, dispensed, and in stock



Monitoring patient safety with the Nplate™ NEXUS Program

The Nplate™ NEXUS Program is designed to promote informed risk-benefit decisions and includes a system of reminders, guides, and databases to monitor patient safety. For instance, the Medication Guide presents information on the risks of Nplate™ in patient-friendly language. Every new patient will be educated on the content of the Medication Guide including the risk-benefit profile of Nplate™.

Healthcare providers submit baseline patient data as patients begin Nplate™ therapy. The purpose of this data collection is to establish the long-term safety and safe use of Nplate™ through periodic monitoring. The registry also includes available baseline patient data.

Twice a year, a NEXUS Specialist will contact the healthcare provider to verify his/her enrolled patient roster and collect safety information. The healthcare provider (or staff under his/her direction) will be asked to complete a safety questionnaire for each patient via fax or phone. This questionnaire asks whether the patient remains on Nplate™ therapy and whether the patient has experienced side effects. The NEXUS Specialist will log any adverse events and discontinuation information into a registry database. Whenever a serious adverse event is reported, someone from the Nplate™ NEXUS Program or Amgen Global Safety will follow up by contacting the reporting provider or representative to obtain additional information.

Please call the Nplate™ NEXUS Program at 1-877-NPLATE1 (1-877-675-2831) to answer any questions or for additional materials. You may also go to www.nplate.com for information and downloadable materials.

Reference: 1. Nplate™ [prescribing information]. Thousand Oaks, CA: Amgen; 2008.





Nplate™ (romiplostim)
Nexus

Network of **EX**perts Understanding and Supporting Nplate™ (romiplostim) and patients

The Nplate™ NEXUS Program connects you with Nplate™ access, support, education, and safety monitoring.

- Amgen is committed to quality patient care. The Nplate™ NEXUS Program is designed to promote informed risk-benefit decisions before initiating treatment and while patients are on treatment to assure appropriate use of Nplate™ and to monitor safety in order to provide quality patient care.

What the Nplate™ NEXUS Program means to you:

- Healthcare provider and patient enrollment
- Education for healthcare providers who intend to prescribe Nplate™, healthcare providers under their direction, and patients
- Monitoring program to manage patient safety

Nplate™ is indicated for the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenic purpura (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Nplate™ should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increases the risk for bleeding. Nplate™ should not be used in an attempt to normalize platelet counts.