



**Medication Policy Manual**

**Policy No:** dru162

**Topic:** Nplate<sup>®</sup>, romiplostim

**Date of Origin:** November 14, 2008

**Revised/Effective Date:** May 12, 2010

**Next Review Date:** May 2011

### **IMPORTANT REMINDER**

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

### **Description**

Romiplostim (Nplate<sup>®</sup>) is a protein that increases platelet production. Although administered subcutaneously, it is not considered a self-administered product due to serious safety concerns. Members who use romiplostim need to be enrolled in a manufacturer-sponsored safety monitoring program.

## **Policy/Criteria**

**I.** Most contracts require prior authorization of romiplostim prior to coverage. Romiplostim may be considered medically necessary in patients with chronic immune (idiopathic) thrombocytopenic purpura (ITP) when all of the following criteria A, B, and C below are met.

**A.** A diagnosis of chronic ITP made by, or in consultation with, a hematologist.

**AND**

**B.** Patient is at risk of spontaneous bleeding as demonstrated in chart notes by either one of the following criteria 1 or 2 below:

**1.** Platelet count less than 20,000/mm<sup>3</sup>.

**OR**

**2.** Platelet count less than 30,000/mm<sup>3</sup> accompanied by symptoms of bleeding.

**AND**

**C.** Treatment with at least one the following ITP treatments was ineffective or not tolerated:

**1.** Adequate course of systemic corticosteroids (e.g., prednisone 1 to 2 mg/kg for 2 to 4 weeks, or pulse dexamethasone 40 mg daily for 4 days).

**OR**

**2.** Immunoglobulin replacement.

**OR**

**3.** Splenectomy.

**II.** Administration, Quantity Limitations, and Authorization Period

**A.** Regence does not consider romiplostim to be a self-administered medication.

**B.** When prior authorization is approved, romiplostim may be initially authorized for a period of 12 weeks.

**C.** Authorization shall be reviewed at least every six months to confirm that the dose does not exceed 10 mcg/kg and the patient's recent (within the last 90 days) platelet count is either:

**1.** Equal to or greater than 30,000/mm<sup>3</sup> but not more than 150,000/mm<sup>3</sup>.

**OR**

**2.** Less than 30,000/mm<sup>3</sup> but platelet counts have increased from baseline accompanied with a resolution of previous bleeding.

**III.** Romiplostim is considered not medically necessary when used for all other conditions, including, but not limited to:

**A.** Acute thrombocytopenia.

**B.** Low platelet counts secondary to other conditions or diseases (including, but not limited to, cancer, HIV, hepatitis, and myelodysplastic syndrome).

**C.** Drug-induced thrombocytopenia (e.g., chemotherapy, heparin).

**D.** Thrombocytopenia secondary to disseminated intravascular coagulation, hemangiomas, or platelet loss (massive bleeding).

**E.** Thrombotic thrombocytopenic purpura/hemolytic-uremic syndrome (TTP/HUS).

## **Position Statement**

### *Summary*

- Romiplostim may maintain platelet counts above 50,000/mm<sup>3</sup> in one-third to one-half of chronic ITP patients and may decrease the need for blood transfusion. It has only been studied in patients for whom traditional treatments have been ineffective. Its value past 24 weeks is still unknown. Romiplostim has a risk of rare but serious side effects that need to be weighed against its potential benefit.
- It is uncertain whether the increase in platelets with romiplostim is sustainable beyond 24 weeks and whether romiplostim decreases bleeding episodes or other complications in patients with chronic ITP.

- A normal platelet count in a healthy person is between 150,000 and 400,000/mm<sup>3</sup>. The goal of treatment for chronic ITP should be to maintain a safe platelet count, not to achieve a normal platelet count. <sup>[1]</sup>
- Risk of spontaneous bleeding increases as platelet counts drops below 20,000 per mm<sup>3</sup>. <sup>[2]</sup>
- Romiplostim is a peptibody used to increase platelet production in patients with chronic ITP who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. <sup>[3]</sup>
- Initial dose of romiplostim is 1 mcg/kg once weekly as a subcutaneous injection. Maximum weekly dose is 10 mcg/kg. <sup>[3]</sup>
- Due to strict monitoring requirement, safety concerns, and lack of data for self-administration, Nplate is currently required to be administered by a health professional.
- Romiplostim is available only through a restricted distribution program called Nplate NEXUS Program. Under the Nplate NEXUS Program, only prescribers and patients registered with the program are able to prescribe, administer, and receive romiplostim.
- Steroids and/or splenectomy are considered first-line treatments of choice for chronic ITP. Other treatments include immune globulin replacement therapy, WinRho, rituximab, danazol, chemotherapy (e.g., Cytosan, Vincristine) and azathioprine. <sup>[4]</sup>
- Around one-third of patients may expect a long-term response from treatment with an oral corticosteroid. Corticosteroids should be rapidly tapered and stopped in patients who fail to respond after 4 weeks. <sup>[5]</sup>
- Up to two-thirds of patients with ITP who undergo splenectomy may achieve a normal platelet count, which is often sustained with no additional therapy. <sup>[4,5]</sup>
- Evidence is reliable that romiplostim increases platelet production to maintain platelet counts over 50,000/mm<sup>3</sup> for 6 of the last 8 weeks of a 24-week trial.
- Romiplostim is linked to uncommon but serious side effects. In an open-label extension study, serious adverse events associated with the use of romiplostim were reported in 9% of patients. <sup>[6]</sup>

### *Clinical Efficacy*

- Romiplostim has been proven in clinical studies to be more effective than placebo.

- \* For every two non-splenectomized patients who received romiplostim, one patient maintained platelet counts above 50,000/mm<sup>3</sup> for 6 weeks during the last 8 weeks of the trial.
- \* For every three splenectomized patients who received romiplostim, one patient maintained platelet counts above 50,000/mm<sup>3</sup> for 6 weeks during the last 8 weeks of the trial.
- There are no studies evaluating the efficacy of romiplostim (Nplate) compared to other standard treatments.

### *Safety*

- Uncommon but serious side effects include:
  - \* **Bone marrow changes:** romiplostim increases the risk for reticulin deposition within the bone marrow. Clinical studies have not ruled out the possibility that reticulin and other fiber deposition may result in bone marrow fibrosis with cytopenias.
  - \* **Worsening low blood platelet count:** discontinuation of romiplostim may result in worsened thrombocytopenia than was present prior to romiplostim therapy.
  - \* **High platelet counts and increased risk of blood clots:** romiplostim may increase platelet counts to a level that produces thrombotic/thromboembolic complications.
  - \* **Worsening hematologic conditions:** romiplostim may increase the risk for hematological malignancies, especially in patients with myelodysplastic syndrome.
- More common adverse reactions are headache, arthralgia, dizziness, insomnia, myalgia, pain in extremity, abdominal pain, shoulder pain, dyspepsia and paresthesia. <sup>[3,7]</sup>

**Appendix A: American Society of Hematology – Criteria for the Diagnosis of Chronic Immune Thrombocytopenic Purpura : Diagnosis of Exclusion**

- History compatible with the diagnosis of chronic ITP
- Normal physical examination findings except for signs of thrombocytopenia (petechiae, purpura, or mucosal bleeding); no adenopathy or splenomegaly
- Complete blood count showing isolated thrombocytopenia with large platelets but no anemia unless bleeding or immune hemolysis is present
- Bone marrow examination showing normal or increased numbers of megakaryocytes (not required for diagnosis unless unusual manifestation or age >60 yr.)
- No clinical or laboratory evidence for other causes of thrombocytopenia

**Cross References**

Immune Globulin Replacement Therapy (IVIG, SQ) dru020

Promacta, eltrombopag dru180

<b>Codes</b>	<b>Number</b>	<b>Description</b>
HCPCS	J2796	Injection, romiplostim, 10 mcg

## References

1. Kojouri K GJ. Recent advances in the treatment of chronic refractory immune thrombocytopenic purpura. *Int J Hematol*. 2005;81(2):119-25. PMID:
2. Marini J, A W. Transfusion and blood component therapy: Lippincott Williams & Wilkins; 2005.
3. Nplate® (Romiplostim) Product Information. Thousand Oaks, CA: Amgen Inc. ; August 2008
4. George JN WS, Raskob GE, et al. Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology. *Blood*. 1996;88:3-40. PMID:
5. Guidelines for the investigation and management of idiopathic thrombocytopenic purpura in adults, children and in pregnancy. *British Journal of Hematology*. 2003;120:574-96. PMID:
6. Newland C SM, Bourgeois E, et al. Evaluating the long-term efficacy of romiplostim (AMG 531) in patients with chronic immune thrombocytopenic purpura (ITP) during an open-label extension study. *Haematologica*. 2008;93(suppl 1)(377 Abstract 0945.). PMID:
7. Nplate® (Romiplostim) Medication guide. Thousand Oaks, CA: Amgen Inc. ; August 2008