POLICY: Thrombocytopenia – Nplate® (romiplostim injection for subcutaneous use – Amgen)

DATE REVIEWED: 03/11/2020

OVERVIEW

Nplate, a thrombopoietin receptor agonist, is indicated for the treatment of thrombocytopenia in adults with chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.[1] Also, Nplate is indicated for use in patients ≥ 1 year of age with ITP for at least 6 months who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Nplate should only be utilized 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. The initial Nplate dose is 1 mcg/kg once weekly as a subcutaneous (SC) injection by a healthcare provider. The dose should be adjusted weekly by increments of 1 mcg/kg to achieve and maintain a platelet count ≥ 50 x 10^9/L as needed to reduce the bleeding risk. Do not exceed a maximum weekly dose of 10 mcg/kg. Discontinue Nplate if the platelet count does not increase after 4 weeks at the maximum dose.

Guidelines

ITP

The guidelines for ITP by ASH were updated in 2019. There are several recommendations. For adults with ITP for at least 3 months who are corticosteroid-dependent or unresponsive to corticosteroid, a thrombopoietin receptor agonist (Promacta® [eltrombopag tablets or oral suspension] or Nplate) or a splenectomy are recommended. In children with newly diagnosed ITP who have non-life-threatening mucosal bleeding, corticosteroids are recommended. For children who have non-life-threatening mucosal bleeding and do not respond to first-line treatment, thrombopoietin receptor agonists are recommended. Other treatment options in children and adults include anti-D immunoglobulin, and rituximab.

Myelodysplastic Syndrome (MDS)

National Comprehensive Cancer Network recommendations regarding MDS (version 2.2020 – February 28, 2020) state to consider treatment with a thrombopoietin receptor agonist in patients with lower-risk MDS who have severe or life-threatening thrombocytopenia.[3] Data are available that describe the use of Nplate in patients with MDS.[4-13] The data with Nplate are discussed noting an increased rate of platelet response and decreased overall bleeding events among patients with low to intermediate risk MDS.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Nplate. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Nplate as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Nplate to be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Nplate is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Chronic Immune Thrombocytopenia.** Approve if the patient meets one of the following criteria (A or B):
   - **A)** Initial Therapy. Approve for 3 months if the patient meets all of the following criteria (i, ii, and iii):
     - **i.** The patient meets one of the following (a or b):
       - **a)** The patient has a platelet count < 30 x 10^9/L (< 30,000/µL); OR
       - **b)** The patient has a platelet count < 50 x 10^9/L (< 50,000/µL) and according to the prescriber the patient is at an increased risk of bleeding; AND
     - **ii.** The agent is prescribed by or in consultation with a hematologist; AND
     - **iii.** The patient meets patient meets one of the following criteria (a or b):
       - **a)** The patient has tried at least one other therapy.
         Note: Examples of therapies are systemic corticosteroids, intravenous immunoglobulin, anti-D immunoglobulin, Promacta® (eltrombopag tablets and oral suspension), Tavalisse™ (fostamatinib tablets), Doptelet® (avatrombopag tablets) and ritixumab; OR
       - **b)** The patient has undergone splenectomy; OR
   - **B)** Continuation of Therapy. Approve for 1 year if the patient meets both of the following criteria: (i and ii):
     - **i.** According to the prescriber the patient demonstrates a beneficial clinical response (e.g., increased platelet counts); AND
     - **ii.** The patient remains at risk for bleeding complications.

   Dosing. Approve up to 10 mcg/kg SC no more frequently than once weekly.

Other Uses with Supportive Evidence

2. **Thrombocytopenia in Myelodysplastic Syndrome**. Approve if the patient meets the following criteria (A or B):
   - **A)** Initial Therapy. Approve for 3 months if the patient meets all the following criteria (i, ii, and iii):
     - **i.** The agent is prescribed by or in consultation with a hematologist or an oncologist; AND
     - **ii.** The patient has low- to intermediate-risk MDS; AND
     - **iii.** The patient meets one of the following (a or b):
       - **a)** The patient has a platelet count < 30 x 10^9/L (< 30,000/µL); OR
       - **b)** The patient has a platelet count < 50 x 10^9/L (< 50,000/µL) and according to the prescriber the patient is at an increased risk of bleeding; OR
   - **B.** Continuation of Therapy. Approve for 1 year if the patient meets both of the following criteria (i and ii):
     - **i.** According to the prescriber the patient demonstrates a beneficial clinical response (e.g., increased platelet counts); AND
     - **ii.** The patient remains at risk for bleeding complications.

   Dosing. Approve up to 1,500 mcg SC no more frequently than twice weekly.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

1. Coverage is not recommended for circumstances not listed in the Authorization Criteria (FDA-approved indications and Other Uses with Supportive Evidence). Criteria will be updated as new published data are available.

REFERENCES

1. Nplate® injection for subcutaneous use [prescribing information]. Thousand Oaks, CA: Amgen, Inc.; October 2019.
2. Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Adv*. 2019;3(23):3829-3866.
3. The NCCN Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (Version 2.2020 – February 28, 2020). © 2019 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed March 9, 2020.
4. Giagounidis A, Mufti GJ, Fenaux P, et al. Results of a randomized, double-blind study of romiplostim versus placebo in patients with low/intermediate-1-risk myelodysplastic syndrome and thrombocytopenia. *Cancer*. 2014;120:1838-1846.
5. Kantarjian HM, Giles FJ, Greenberg PL, et al. Phase 2 study of romiplostim in patients with low- or intermediate-risk myelodysplastic syndrome receiving azacitidine therapy. *Blood*. 2010;116(17):3163-3170.
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10. Wang ES, Lyons RM, Larson RA, et al. A randomized, double-blind, placebo-controlled phase 2 study evaluating the efficacy and safety of romiplostim treatment of patients with low or intermediate-1 risk myelodysplastic syndrome receiving lenalidomide. *J Hematol Oncol*. 2012;5:71.
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12. Brierley CK Steensma DP. Thrombopoiesis-stimulating agents and myelodysplastic syndromes. *Br J Haematol*. 2015;169:309-323.
13. Prica A, Sholzberg M, Buckstein R. Safety and efficacy of thrombopoietin-receptor agonists in myelodysplastic syndromes: a systematic review and meta-analysis of randomized controlled trials. *Br J Haematol*. 2014;167:626-638.

HISTORY

Type of Revision	Summary of Changes	Date Reviewed
New policy	--	01/30/2019
Early annual revision	The following criteria changes were made. 1. **Chronic Immune Thrombocytopenia:** The approval duration was changed from 3 year to 1 year. Doptelet was added to the list of alternatives that count towards the criteria that requires a trial of one other therapy. The dosing was changed to approve up to 10 mcg/kg SC no more frequently than once weekly. 2. **Myelodysplastic Syndrome:** Dosing was changed to approve up to 1,500 mcg SC no more frequently than twice weekly.	07/03/2019
Early annual revision	The following criteria changes were made: 1. **Chronic Immune Thrombocytopenia:** Criteria were divided into Initial Therapy and Continuation of Therapy. For Initial Therapy, the approval duration was changed from 3 months to 1 year. Criteria were added that the patient has a platelet count < 30 x 10^9/L (< 30,000/µL) or that the patient has a platelet count < 50 x 10^9/L (< 50,000/µL) and, according to the prescriber, the patient is at an increased risk of bleeding. Also, regarding the requirement of a trial of at least one therapy, the descriptor "systemic" was added in reference to corticosteroids. Continuation of therapy is approved for a 1-year duration if, according to the prescriber, the patient demonstrates a beneficial clinical response (e.g., increase in platelet counts) and the patient remains at risk for bleeding complications. 2. **Thrombocytopenia in Myelodysplastic Syndrome:** Criteria were divided into Initial Therapy and Continuation of Therapy. For Initial Therapy, the approval duration was changed from 1 year to 3 months. Criteria were changed that the patient has a platelet count < 30 x 10^9/L (< 30,000/µL) or that the patient had a platelet count < 50 x 10^9/L (< 50,000/µL) and, according to the prescriber, the patient is at an increased risk of bleeding. Previously, the criteria just required that the patient had clinically significant thrombocytopenia (e.g., low platelet counts [< 30 x 10^9/L {< 30,000/µL} {pretreatment}]; is platelet transfusion-dependent; active bleeding, and/or a history of bleeding at low platelet counts). Continuation of therapy is approved for a 1-year duration, if according to the prescriber, the patient demonstrates a beneficial clinical response (e.g., increase in platelet counts) and the patient remains at risk for bleeding complications).	03/11/2020

SC – Subcutaneously.