Reference number(s)
3371-A

STANDARD MEDICARE PART B MANAGEMENT

NPLATE (romiplostim)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Nplate is indicated for the treatment of thrombocytopenia in:
      i. Adult patients with immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.
      ii. Pediatric patients 1 year of age and older with ITP for at least 6 months who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.
   2. Nplate is indicated to increase survival in adults and in pediatric patients (including term neonates) acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome [HS-ARS]).

B. Compendial Uses
   1. Myelodysplastic syndromes, for lower risk disease in patients with severe or refractory thrombocytopenia following disease progression or no response to hypomethylating agents, immunosuppressive therapy
   2. Chemotherapy-induced thrombocytopenia (CIT)

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. DOCUMENTATION

The following documentation must be available, upon request, for all submissions for immune thrombocytopenia and chemotherapy-induced thrombocytopenia (CIT):
A. For initial requests: pretreatment platelet count
B. For continuation requests: current platelet count

III. CRITERIA FOR INITIAL APPROVAL

A. Immune Thrombocytopenia (ITP)
Authorization of 12 months may be granted for treatment of ITP when both of the following criteria are met:
   1. Untransfused platelet count at any point prior to the initiation of the requested medication is less than $30x10^9$/L OR $30x10^9$/L to $50x10^9$/L with symptomatic bleeding (e.g., significant mucous membrane

bleeding, gastrointestinal bleeding or trauma) or risk factors for bleeding (e.g., undergoing a medical or dental procedure where blood loss is anticipated, comorbidities such as peptic ulcer disease and hypertension, mandated anticoagulation therapy, profession [e.g., construction worker] or lifestyle [e.g., plays contact sports] that predisposes patient to trauma).

2. At least one of the following criteria is met:
   i. The member has previously received treatment with an immunoglobulin for the treatment of ITP.
   ii. The member had an inadequate response to corticosteroids.
   iii. There is a clinical reason to avoid treatment with both immunoglobulins and corticosteroids.
   iv. The member has undergone a splenectomy.

B. Hematopoietic syndrome of acute radiation syndrome (HS-ARS)

Authorization of 1 month may be granted for treatment of hematopoietic syndrome of acute radiation syndrome (acute exposure to myelosuppressive doses of radiation).

C. Myelodysplastic Syndromes

Authorization of 12 months may be granted for treatment of myelodysplastic syndromes with severe or refractory thrombocytopenia when both of the following criteria are met:

1. Member has lower risk disease defined as Revised International Prognostic Scoring System (IPSS-R) (Very Low, Low, Intermediate), International Prognostic Scoring System (IPSS) (Low/Intermediate-1), WHO classification-based Prognostic Scoring System (WPSS) (Very Low, Low, Intermediate).
2. Member has severe or refractory thrombocytopenia following disease progression or no response to hypomethylating agents (such as azacitidine and decitabine), or immunosuppressive therapy.

D. Chemotherapy-induced thrombocytopenia

Authorization of 6 months may be granted for treatment of chemotherapy-induced thrombocytopenia (CIT) when either of the following criteria are met:

1. The platelet count is less than $100x10^9$/L for at least 3-4 weeks following the last chemotherapy administration.
2. Chemotherapy administration has been delayed related to thrombocytopenia.

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

A. Immune Thrombocytopenia (ITP)

Authorization may be granted when all of the following criteria are met:

1. The member is currently receiving therapy with Nplate.
2. Nplate is being used to treat immune thrombocytopenia (ITP).
3. Either of the following criteria is met:
   i. Authorization of 12 months may be granted for members receiving benefit from therapy. Benefit is defined as any of the following:
      a. Current platelet count less than $50x10^9$/L for whom the current platelet count is sufficient to prevent clinically important bleeding.
      b. Current platelet count of $50x10^9$/L to $200x10^9$/L.
      c. Current platelet count greater than $200x10^9$/L to less than or equal to $400x10^9$/L for whom Nplate dosing will be adjusted to achieve a platelet count sufficient to avoid clinically important bleeding.

ii. Authorization of 3 months may be granted for members with current platelet count less than $50x10^9$/L for whom the current platelet count is not sufficient to prevent clinically important bleeding and who have not received a maximal Nplate dose for at least 4 weeks.

B. Myelodysplastic Syndromes

Authorization for 12 months may be granted when all of the following criteria are met:

1. The member is currently receiving therapy with Nplate.
2. Nplate is being used to treat myelodysplastic syndromes (MDS).
3. The member is receiving benefit from therapy. Benefit is defined as any of the following:
   i. Increased platelet counts
   ii. Decreased bleeding events
   iii. Reduced need for platelet transfusions

C. Chemotherapy-Induced Thrombocytopenia

Authorization for 12 months may be granted when all of the following criteria are met:

1. The member is currently receiving therapy with Nplate.
2. Nplate is being used to treat chemotherapy-induced thrombocytopenia (CIT).
3. The member is receiving benefit from therapy. Benefit is defined as any of the following:
   i. Increased platelet counts
   ii. Decreased bleeding events
   iii. Reduced need for platelet transfusions
4. The requested drug is used to maintain dose schedule and intensity of chemotherapy.[10]

V. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:

1. The prescribing information for Nplate.
2. The available compendium
   a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
   b. Micromedex DrugDex
   c. American Hospital Formulary Service- Drug Information (AHFS-DI)
   d. Lexi-Drugs
   e. Clinical Pharmacology
3. NCCN Guideline: Hematopoietic growth factors
4. NCCN Guideline: Myelodysplastic syndromes
5. American Society of Hematology 2019 guidelines for immune thrombocytopenia.
6. Updated international consensus report on the investigation and management of primary immune thrombocytopenia.

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Nplate are covered in addition to the following:

1. Severe or refractory thrombocytopenia in myelodysplastic syndromes
2. Treatment of chemotherapy-induced thrombocytopenia (CIT)

VI. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

The safety and efficacy of romiplostim were assessed in 2 double-blind, placebo-controlled clinical studies of 125 adult patients with chronic ITP and in an open-label extension study. In these studies, treatment with romiplostim resulted in dose-dependent increases in platelet counts. After a single subcutaneous dose of 1 to 10 mcg/kg of romiplostim, the peak platelet count was 1.3 to 14.9 times greater than the baseline platelet count over a 2- to 3-week period. The platelet counts were above 50 x 10^9/L for 7 out of 8 patients with chronic ITP who received 6 weekly doses of romiplostim at 1 mcg/kg.

Kuter et al. (2008) assessed the long-term effects of romiplostim in splenectomized and non-splenectomized patients with ITP in 2 parallel trials. A total of 63 splenectomized and 62 non-splenectomized patients with ITP with a mean of 3 platelet counts of 30 x 10^9/L or less were randomly assigned 2:1 to subcutaneous injections of romiplostim (n = 42 in the splenectomized study and n = 41 in the non-splenectomized study) or placebo (n = 21 in both studies) every week for 24 weeks. Doses of romiplostim were adjusted to maintain platelet counts of 50 x 10^9/L to 200 x 10^9/L. The primary objectives were to assess the efficacy of romiplostim as measured by a durable platelet response (platelet count greater than or equal to 50 x 10^9/L during 6 or more of the last 8 weeks of treatment) and treatment safety. The authors reported that a durable platelet response was achieved by 38% (16/42) of the splenectomized patients given romiplostim versus none (0/21) of the placebo patients, and by 61% (25/41) of the non-splenectomized patients given romiplostim versus 0.05% (1/21) given placebo. Eighty-seven percent (20/23) of patients given romiplostim (12/12 splenectomized and 72% (8/11) non-splenectomized patients) reduced or discontinued concurrent therapy compared with 38% (6/16) of those given placebo (1/6 splenectomized and 5/10 non-splenectomized patients). Adverse events were reported to be similar in both groups. Furthermore, no antibodies against romiplostim or thrombopoietin were detected. The authors concluded that romiplostim was well-tolerated and increased and maintained platelet counts in splenectomized and non-splenectomized patients with ITP and that many patients were able to reduce or discontinue other ITP medications.

Following completion of the placebo-controlled studies, 100 patients entered an extension study of long-term romiplostim therapy. The majority of patients maintained platelet counts of 50,000/mcL or greater throughout the study with a median duration of romiplostim treatment of 60 weeks and a maximum duration of 96 weeks. Support for using Nplate for severe or refractory thrombocytopenia can be found in the American Society of Hematology guidelines for immune thrombocytopenia and the International Consensus Report on the investigation and management of primary immune thrombocytopenia.

Initial treatment for newly-diagnosed adults consists of corticosteroids such as dexamethasone and prednisone and immunoglobulins. Subsequent treatment includes rituximab, eltrombopag, avatrombopag, romiplostim. Subsequent medical treatment options with less robust evidence include azathioprine, cyclophosphamide, cyclosporine A, danazol, dapsone, mycophenolate mofetil, and vinca alkaloids. Splenectomy is recommended as subsequent treatment.

The goal of treatment is to prevent severe bleeding episodes. According to Provan et al. (2019), treatment should maintain a target platelet level of more than 20-30 x 10^9/L at least for symptomatic patients because risk for major bleeding increases below this level. In the studies cited in the package insert, a durable platelet response was the achievement of a weekly platelet count ≥ 50 × 10^9/L for any 6 of the last 8 weeks of the 24-week treatment period in the absence of rescue medication at any time. A transient platelet response was the achievement of any weekly platelet counts ≥ 50 × 10^9/L for any 4 weeks during the treatment period without a durable platelet response. An overall platelet response was the achievement of either a durable or a transient platelet response.

Support for using Nplate in myelodysplastic syndromes can be found in the National Comprehensive Cancer Network's guideline for myelodysplastic syndrome. The NCCN Guideline supports the use of Nplate for treatment of lower risk disease in patients with severe or refractory thrombocytopenia following disease

progression or no response to hypomethylating agents or immunosuppressive therapy. Lower risk myelodysplastic syndrome is defined as Revised International Prognostic Scoring System (IPSS-R) category very low, low, or intermediate.

Support for chemotherapy-induced thrombocytopenia can be found in the National Comprehensive Cancer Network's guideline for hematopoietic growth factors. The NCCN Guideline for hematopoietic growth factors supports the use of Nplate for treatment of chemotherapy-induced thrombocytopenia (CIT). Patients should have platelets less than 100,000/mcL for at least three to four weeks following the last chemotherapy administration and/or following delays in chemotherapy initiation related to thrombocytopenia.

VII. REFERENCES

1. Nplate [package insert]. Thousand Oaks, CA: Amgen Inc.; February 2022.
2. Nuenert C, Terrel DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Adv.* 2019;3(23):3829–3866.
3. Provan D, Arnold DM, Bussel JB, et al. Updated international consensus report on the investigation and management of primary immune thrombocytopenia. *Blood Adv.* 2019;3(22): 3780–3817.
4. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed June 2, 2023.
5. The NCCN Clinical Practice Guidelines in Oncology® Myelodysplastic Syndrome (Version 1.2023). © 2023 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed June 2, 2023.