Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 04/11/2024

Nplate® (romiplostim)

HCPCS: J2796

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved age
   b. Diagnosis confirmed by, or in consultation with, a hematologist
   c. For immune thrombocytopenic purpura (ITP)
      i. Diagnosis of ITP defined by the following:
         1. Thrombocytopenia (platelet count < 100,000/mcL)
            a) Current platelet count < 20,000/mcL
               OR
            b) Current platelet count < 30,000/mcL AND symptoms of active bleeding
      ii. Inadequate response to therapy with corticosteroids, immunoglobulins, or splenectomy
      iii. Dose is ≤ 10 mcg/kg/week

      OR
   d. A diagnosis of hematopoetic syndrome of acute radiation syndrome (HS-ARS)
   e. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period:
      i. For ITP: Three months initially. Continuation of therapy to be reviewed annually
      ii. For HS-ARS: 60 days approval to allow for one time administration
   c. Renewal Criteria:
      i. For ITP:
         1. Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit
         2. Recent platelet count of 30,000-150,000/mcL
         3. Dose is ≤ 10 mcg/kg/week
      ii. For HS-ARS:

1. Not applicable as no further authorization will be provided

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Nplate is a thrombopoietin receptor agonist indicated for the treatment of thrombocytopenia in adult patients with ITP who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy and 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. Nplate is also indicated to increase survival in adults and in pediatric patients (including term neonates) acutely exposed to myelosuppressive doses of radiation (HS-ARS).

- Nplate is not indicated for the treatment of thrombocytopenia due to myelodysplastic syndrome (MDS) or any cause of thrombocytopenia other than ITP. 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.

- Idiopathic thrombocytopenic purpura

    - ITP, also known as primary immune thrombocytopenic purpura, is an autoimmune, hematologic disorder characterized by persistent thrombocytopenia due to autoantibody binding to platelet antigen(s) causing their premature destruction leading to an increase in bruising and bleeding. Risk of spontaneous bleeding increases as platelet counts drops below 20,000/mm^3. There are estimated to be approximately 60,000 individuals diagnosed with chronic ITP in the U.S.

    - For all patients with severe bleeding (eg, intracranial, gastrointestinal) and a platelet count < 30,000/microL, it is recommended that immediate platelet transfusion along with ITP-specific therapy with intravenous immune globulin (IVIG) and high-dose glucocorticoids. Recommendations also suggest ITP-specific therapy for patients with a new diagnosis of ITP and a platelet count < 20,000/microL, even in the absence of bleeding symptoms, because the thrombocytopenia may be persistent and become more severe. Some patients with platelet counts > 30,000/microL may require treatment if they have an increased risk of bleeding (eg, peptic ulcer disease, high risk of falling), other hemostatic defects (eg, use of antiplatelet agents or anticoagulants), a history of bleeding at a higher platelet count, or a need for surgery/invasive procedures.

    - Per the American Society of Hematology (ASH) guidelines for immune thrombocytopenia (2019) it is recommended that patients with ITP for ≥ 3 months who are corticosteroid-dependent or unresponsive to corticosteroids and are going to be treated with a TPO-RA, both eltrombopag and romiplostim (Nplate®) are suggested recommendations, with no clinical preference between the two. Doptelet® (avatrombopag) is another TPO-RA approved in 2018 for ITP and is not included in these guidelines. These guidelines make weak recommendations for a TPO-RA over rituximab and for rituximab over splenectomy, but the guideline emphasizes the potential usefulness of all three treatments. Tavalisse® (fostamatinib) is another treatment option that is not included in the ASH guidelines that is often used after a trial of guideline recommended therapies.

- First-line therapy is comprised of oral corticosteroids, immunoglobulins, and splenectomy. These therapies may be undesirable due to the associated complications and/or failure to achieve desirable response. Nplate, administered subcutaneously, is a peptibody that binds to and activates the human thrombopoietin receptor (TPO) leading to increased platelet production.

- Hematopoietic syndrome of acute radiation syndrome

    - Acute Radiation Syndrome (ARS) (sometimes known as radiation toxicity or radiation sickness) is an acute illness caused by irradiation of the entire body (or most of the body) by a high dose of penetrating radiation in a very short period of time (usually a matter of minutes).

    - The type of radiation exposure event influences the nature of the exposure (i.e., nonionizing versus ionizing radiation), types of ionizing particles (eg, alpha particles, beta particles, neutrons) and/or x-ray/gamma rays, the amount and duration of radiation exposure, and the consequent biologic effects.

    - Hematopoietic syndrome (sometimes referred to as bone marrow syndrome) will usually occur with a dose between 0.7 and 10 Gray (Gy: derived unit of ionizing radiation dose in the International System of Units (SI). It is defined as the absorption of one joule of radiation energy per kilogram of matter.)

        - Prodromal symptoms include anorexia, nausea and vomiting. Latent stage includes death of stem cells in bone marrow which can manifest symptoms of anorexia, fever, and malaise with a drop in all blood cell counts causing infection and hemorrhage.

    - The recommended dose of Nplate is 10 mcg/kg administered once as a subcutaneous injection, and the dose should be administered as soon as possible after suspected or confirmed exposure to radiation levels greater than 2 Gy. Nplate should be administered regardless of whether a complete blood count can be obtained. The patient's absorbed whole body radiation dose should be estimated based on information from public health authorities, biodosimetry if available, or clinical findings such as time to onset of vomiting or lymphocyte depletion kinetics.

    - Efficacy studies of Nplate could not be conducted in humans with acute radiation syndrome for ethical and feasibility reasons. Efficacy studies conducted in animals, Nplate's effect on platelet count in healthy human volunteers and its effect on thrombocytopenia in patients with ITP lead to its approval. Nplate significantly increased 60-day survival in irradiated animals. 72.5% survival in the Nplate group compared to 32.5% survival in the control group after total body irradiation of 6.8 Gy.

References:

1. Kojouri K GJ. Recent advances in the treatment of chronic refractory immune thrombocytopenic purpura. Int J Hematol. 2005;81(2):119-25.
2. Marini J, A W. Transfusion and blood component therapy: Lippincott Williams & Wilkins; 2005.
3. Nplate® (Romiplostim) Product Information. Thousand Oaks, CA: Amgen Inc.; February, 2021.
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.
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.
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.).
7. Promacta® (eltrombopag) Product Information. Research Triangle Park, NC: GlaxoSmithKline; November 2018.

8. Kuter DJ, Rummel M, Boccia R, Macik BG, Pabinger I, Selleslag D, Rodeghiero F, Chong BH, Wang X, Berger DP. Romiplostim or standard of care in patients with immune thrombocytopenia. N Engl J Med. 2010 Nov 11;363(20):1889-99.
9. 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 Oct 28;116(17):3163-70. Epub 2010 Jul 14.
10. Feudjo-Tepie M, Robinson N, Bennett D. Prevalence estimates of adult chronic idiopathic thrombocytopenic purpura (ITP). J Thromb Haemost. 2008;6(4):711-712
11. © 2012 RegenceRx – Nplate (romiplostim). June 2012.
12. FDA Drug Safety Communication: Modified Risk Evaluation and Mitigation Strategies (REMS)for Nplate (romiplostim) and Promacta (eltrombopag). accessed 2/26/13 Available from: http://www.fda.gov/Drugs/DrugSafety/ucm280165.htm.
13. Radiation Emergencies. Acute radiation syndrome: A fact sheet for clinicians. Centers for Disease Control and Prevention https://www.cdc.gov/nceh/radiation/emergencies/arsphysicianfactsheet.htm Accessed March 2021.
14. Allen JY, Wingard JR, Kainiak N. Management of radiation injury. UpToDate. Literature review current through 2/2021. https://www.uptodate.com/contents/management-of-radiation-injury Accessed March 2021
15. Cindy E. Neunert; Current management of immune thrombocytopenia. Hematology Am Soc Hematol Educ Program 2013; 2013 (1): 276–282. doi: https://doi.org/10.1182/asheducation-2013.1.276
16. George JN, Arnold DM. Immune thrombocytopenia (ITP) in adults: Second-line and subsequent therapies. UpToDate. Current through October 2020. https://www.uptodate.com/contents/immune-thrombocytopenia-itp-in-adults-second-line-and-subsequent-therapies accessed November 2020.
17. Cindy Neunert, Deirdra R. Terrell, Donald M. Arnold, et. al.; American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Adv 2019; 3 (23): 3829–3866. doi: https://doi.org/10.1182/bloodadvances.2019000966

Policy History		
#	Date	Change Description
2.5	Effective Date: 04/11/2024	Annual review of criteria was preformed, no changes were made
2.4	Effective Date: 04/06/2023	Updated the approval duration for HS-ARS to allow for 60 day requirement
2.3	Effective Date: 04/14/2022	Annual review of criteria was performed, no changes were made.
2.2	Effective Date: 04/08/2021	Updated with new FDA indication for hematopoetic syndrome of acute radiation syndrome (HS-ARS)
2.1	Effective Date: 12/03/2020	Annual review of criteria was performed, no changes were made.
2.0	Effective Date: 12/05/2019	Updated with new indication
1.9	Effective Date: 02/14/2019	Updated with new FDA age requirements
1.8	Effective Date: 02/08/18	Annual review of criteria was performed, no changes were made.

<table>
<tr><td>1.7</td><td>Effective Date: 07/05/17</td><td>UM medical management system update for MAPPO and BCNA
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table></td></tr>
<tr><td>1.6</td><td>Effective Date: 02/09/17</td><td>Annual review of criteria was performed, no changes were made.</td></tr>
<tr><td>1.5</td><td>Effective Date: 01/01/16</td><td>Updated with specific products required</td></tr>
<tr><td>1.4</td><td>Effective Date: 10/20/14</td><td>Added requirement of trial and failure of a preferred product</td></tr>
<tr><td>1.3</td><td>Effective Date: 08/14/14</td><td>Updated platelet requirements</td></tr>
<tr><td>1.2</td><td>Effective Date: 04/01/14</td><td>UM medical management system update for BCBS and BCN
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table></td></tr>
<tr><td>1.1</td><td>Effective Date: 05/02/13</td><td>Removed REMS requirement</td></tr>
<tr><td>1.0</td><td>Effective Date: 01/20/09</td><td>New Policy</td></tr>
</table>

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm*

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form
Nplate® (romiplostim) HCPCS CODE: J2796

Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

This form is to be used by participating physicians to obtain coverage for Nplate. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	**Name**
ID Number	**Specialty**
D.O.B. ☐Male ☐Female **Pt weight (in kg)** **Date recorded:** _____	**Address**
Diagnosis	**City /State/Zip**
Drug Name	**Phone/Fax: P**: ( ) - **F**: ( ) -
Dose and Quantity	**NPI**
Directions	**Contact Person**
Date of Service(s)	**Contact Person Phone / Ext.**

STEP 1: DISEASE STATE INFORMATION

1. Initiation or Continuation of treatment? ☐ Initiation ☐ Continuation *Date patient started therapy:* _____

2. Please provide the NPI number for the place of administration: _____

3. **Initiation and Continuation of therapy:**
   a. Please check the patient's diagnosis:
      ☐ Immune Thrombocytopenia Purpura (ITP)
      ☐ Hematopoietic syndrome of acute radiation syndrome (HS-ARS)
      ☐ Other _____
   b. What is the patient's current platelet thousands of cells/microliter (K/mcL))? _____ Date: _____
   c. Does the patient have symptoms of active bleeding prior to initiation of treatment?
      ☐ Yes ☐ No, Please explain the symptoms of active bleeding: _____
   d. Which of the following medications or procedure has the patient previously been treated with and had an inadequate response?
      ☐ Corticosteroids
      ☐ Immunoglobulins
      ☐ Splenectomy
      ☐ Other _____

4. **Continuation request** (please fill out above section as well): Nplate **start date** _____
   a. **For ITP:** What is the patient's current platelet count in cells/microliter (mcL)?
      _____ Date: _____
   b. **For HS-ARS**: Please include rationale for continuation of therapy_____

Please add any other supporting medical information necessary for our review

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name **Physician Signature** **Date**

Step 2: Checklist	☐ Form Completely Filled Out ☐ Attached Chart Notes	☐ Weight (specify lb or kg), BSA ☐ Response Assessment
Step 3: Submit	**By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979**	**By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320**

01/21/14; 03/26/14; 09/22/14; 2/2/2018;10/11/2018; 1/31/2020; 3/17/2020; 4/8/2021