Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION AND STEP THERAPY POLICY AND CRITERIA ORPTCHEM034.1225	**HEMATOLOGICAL AGENTS** **THROMBOCYTOPENIA MEDICATIONS** **Nplate®** (romiplostim SQ injection)
Effective Date: 2/1/2026	**Review/Revised Date**: 11/22 , 11/23, 10/24, 11/25 (KN)
Original Effective Date: 08/15	**P&T Committee Meeting Date**: 12/21, 12/22, 12/23, 12/24, 12/25
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:
Providence Health Plan and Providence Health Assurance as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:
Medicare Part B

POLICY CRITERIA:

COVERED USES:
All Food and Drug Administration (FDA)-Approved Indications, some medically accepted Indications.

REQUIRED MEDICAL INFORMATION:
For initiation of therapy, must meet indication-specific criteria below:

1. For **Oncologic Diagnoses:** Use must be for an FDA approved indication or indication supported by National Comprehensive Cancer Network guidelines with recommendation 2A or higher
2. For **Immune Thrombocytopenia (ITP)**, Nplate®, may be covered if all the following criteria are met**:**
    a. Documented risk for bleeding as indicated by at least one of the following:
        i. Severe ITP (bleeding symptoms)
        ii. Risk factors for bleeding are present (such as uncontrolled hypertension, active peptic ulcer disease, anticoagulation, recent surgery, head trauma)
        iii. In preparation for procedures or surgery with risk of bleeding
        iv. Professional or lifestyle risk factors for trauma
    b. Persistent or chronic disease (greater than 6 months)
    c. Documented lack of response (defined as platelet count less than 30,000 cells per microliter or less than 2-fold increase in baseline platelets) to at least one of the following:
        i. Corticosteroids in a dosing regimen standard for ITP treatment

   ii. Intravenous Immune globulin (IVIg) with documentation of either a need for rapid response (<48 hours) or an intolerance or contraindication to corticosteroids
   iii. Intravenous anti-D in patients who are Rh positive and non-splenectomized with documentation of either a need for rapid response (<48 hours) or an intolerance or contraindication to corticosteroids
3. For **Hematopoietic Syndrome of Acute Radiation Syndrome [HSARS]**, Nplate® may be covered if the patient has suspected or confirmed exposure to radiation levels greater than 2 gray (Gy)

For patients established on therapy, must meet indication-specific criteria below:
1. For **ITP:**
   a. Documentation of response to therapy (defined as platelet count of at least 30,000 cells per microliter or a 2-fold increase in baseline platelets)
2. For **HSARS**: Members must meet the initial approval criteria above for each request

EXCLUSION CRITERIA:
Concomitant use with other thrombopoietin receptor agonists (e.g., Mulpleta®, Promacta®) or with tyrosine kinase inhibitors (e.g., Tavalisse®, Wayrilz®).

AGE RESTRICTIONS: N/A

PRESCRIBER RESTRICTIONS:
Must be prescribed by, or in consultation with, an oncologist, hematologist, gastroenterologist or hepatologist.

COVERAGE DURATION:
- For **ITP**: Initial authorization will be approved for six months. Reauthorization will be approved for one year
- For **HSARS**: Authorization will be approved for three months

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Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION:

Thrombocytopenia is a condition characterized by a low blood platelet count. Platelets (thrombocytes) are colorless blood cells that help blood clot. Thrombopoietin receptor agonists (TPO-RAs; e.g., Mulpleta®, Promacta®, Nplate®) and spleen tyrosine kinase (SYK) inhibitors (e.g., Tavalisse®) are medications used to treat thrombocytopenia when standard therapies, such as corticosteroids, are not sufficient. TPO-RAs increases the production of platelets by stimulating bone marrow cells, whereas the SYK inhibitors work by preventing the breakdown of platelets.

FDA APPROVED INDICATIONS:

- Pediatric patients one year of age and older with immune thrombocytopenia (ITP) for at least six months who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy
- Adults with immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy
- 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 [HSARS])

POSITION STATEMENT:

Immune Thrombocytopenia (ITP)

ITP is an autoimmune disorder characterized by isolated thrombocytopenia (low blood platelet count) with otherwise normal complete blood count in the absence of other apparent causes (i.e., associated conditions, drugs). The main clinical manifestations of ITP are related to excessive bleeding, which is typically mucocutaneous including petechiae, purpura, easy bruising, epistaxis, gingival bleeding, and menorrhagia. More overt bleeds such as gastrointestinal bleeds, gross hematuria, and intracranial hemorrhage are rare.

The American Society of Hematology (ASH) 2019 guidelines recommend short courses of corticosteroids (less than or equal to six weeks) as first-line treatment. Intravenous immunoglobulin (IVIg) either as single agent or in combination with corticosteroids may also be appropriate. Second-line treatments include splenectomy, TPO-receptor agonists (e.g., eltrombopag, romiplostim), and rituximab. Splenectomy is the only treatment that provides sustained remission off all treatments at one year and beyond in a high proportion of ITP patients. The goal in

treatment of ITP is not to achieve a normal platelet count but a safe level that avoids bleeding.

Evidence of romiplostim (Nplate®) in chronic ITP

- The safety and efficacy of romiplostim in adults with ITP were assessed in two double-blind, placebo-controlled clinical studies, an open-label single-arm study, and in an open-label extension study.
- In the two double-blind, placebo-controlled clinical studies (Studies 1 and 2), patients with ITP who had completed at least one prior treatment and had a platelet count of ≤ 30 × 109/L prior to study entry were randomized (2:1) to 24 weeks of romiplostim (1 mcg/kg subcutaneous [SC]) or placebo given weekly. Prior ITP treatments in both study groups included corticosteroids, immunoglobulins, rituximab, cytotoxic therapies, danazol, and azathioprine. Patients already receiving ITP medical therapies at a constant dosing schedule were allowed to continue receiving these medical treatments throughout the studies. Rescue therapies (i.e., corticosteroids, IVIG, platelet transfusions, and anti-D immunoglobulin) were permitted for bleeding, wet purpura, or if the patient was at immediate risk for hemorrhage.
    - Study 1 evaluated patients who had ***not*** undergone a splenectomy. The patients had been diagnosed with ITP for approximately 2 years and had received a median of three prior ITP treatments. Overall, the median platelet count was 19 × 10^9/L at study entry. During the study, the median weekly romiplostim dose was 2 mcg/kg
    - Study 2 evaluated patients who had undergone a splenectomy. The patients had been diagnosed with ITP for approximately 8 years and had received a median of six prior ITP treatments. Overall, the median platelet count was 14 × 10^9/L at study entry. During the study, the median weekly romiplostim dose was 3 mcg/kg
    - The results showed that 88% and 79% of patients in the romiplostim groups of Studies 1 and 2 achieved an overall platelet response (platelet counts of ≥ 50 × 109/L in any four weeks of the 24-week study period) versus 14% and 0% in the placebo group respectively. Durable platelet response (platelet counts of ≥ 50 × 109/L in any six of the last eight weeks of the 24-week study period) was achieved in 61% and 38% of patients in the romiplostim groups, versus 5% and 0% in placebo, respectively.

Hematopoietic Syndrome of Acute Radiation Syndrome (HSARS)

Hematopoietic Syndrome of Acute Radiation Syndrome (HSARS) occurs in adult and pediatric patients exposed to myelosuppressive doses of radiation. Symptoms include nausea, vomiting, diarrhea, headache, weakness, or drop in blood counts.

Romiplostim garnered approval for this indication based on efficacy studies conducted in animals, effect on platelets counts in health human volunteers, and effect on thrombocytopenia in patients with ITP for ethical and feasibility reasons. The animal study was a randomized, blinded, placebo-controlled study in Rhesus monkeys exposed to a total body irradiation of 6.8 Gy from a $Cobalt^{60}$ gamma ray source, representing a dose that would be lethal in 70% of animals by 60 days of follow-up (LD70/60). They were then administered either a single subcutaneous dose of blinded treatment (control article [sterile saline] or romiplostim [5 mg/kg]) 24 hours post-irradiation

- The primary endpoint was survival was statistically significant for romiplostim treated group. 72.5% survival (29/40) in the romiplostim group compared to 32.5% survival (13/40) in the control group
    - An exploratory cohort of n=40 animals received romiplostim (5 mg/kg) on day one and pegfilgrastim (0.3 mg/kg) on days one and eight post-irradiation.
    - Combined treatment group survival was 87.5% (95% CI: (73.2%, 95.8%)).
- The safety was assessed based on the clinical experience in patients with ITP and from healthy volunteers.
- The 10 mcg/kg dosing regimen for humans is based on population modeling and simulation analyses.

BILLING GUIDELINES AND CODING:

CODES*		
HCPCS	J2796	Injection, romiplostim, 10 micrograms
CPT	96372	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular

*Coding Notes:
• The above code list is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit.
• HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as “medically unlikely edits” (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

REFERENCE/RESOURCES:

1. Nplate® (romiplostim) package insert. Thousand Oaks, CA: Amgen; 2022 February.
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.Erratum in: *Blood Adv*. 2020;4(2):252.

3. Barnett CL, Mladsi D, Vredenburg M, Aggarwal. Journal of Medical Economics. 2018; 21:8, 827-834.
4. Stasi R. How to approach thrombocytopenia. American Society of Hematology Education Book 2012; 2012(1):191-197.
5. Kuter DJ, Bussel JB, Lyons RM, et al. Efficacy of romiplostim in patients with chronic immune thrombocytopenia purpura: a double-blind randomized controlled trial. *Lancet.* 2008 Feb 2; 371(9610):395-403.
6. Newland C, Sanz MA, 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.
7. Kistangari G, McCrae KR. Immune thrombocytopenia. Hematol Oncol Clin North Am. 2013;27(3):495-520. doi: 10.1016/j.hoc.2013.03.001.