# Drug Coverage Policy

**Effective Date ..... 8/1/2024**
**Coverage Policy Number.....IP0155**
**Policy Title.....Nplate**

# Thrombocytopenia – Nplate

- Nplate® (romiplostim subcutaneous injection – Amgen)

***INSTRUCTIONS FOR USE***
*The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.*

## Cigna Healthcare Coverage Policy

Nplate, a thrombopoietin receptor agonist, is indicated for the treatment of:[1]

- **Hematopoietic syndrome of acute radiation syndrome**, to increase survival in adults and pediatric patients (including term neonates) acutely exposed to myelosuppressive doses of radiation.
- **Immune thrombocytopenia (ITP), in adults** who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.
- **Immune thrombocytopenia (ITP), in pediatric 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.[1] Nplate should not be used in an attempt to normalize platelet counts.

**Guidelines**
Nplate is mentioned in various clinical guidelines.

- **Chemotherapy Induced Thrombocytopenia:** The National Comprehensive Cancer Network (NCCN) guidelines for hematopoietic growth factors (version 3.2024 – January 30, 2024) recommend consideration of Nplate for the management of suspected chemotherapy induced thrombocytopenia (category 2A) in addition to other modalities (e.g., platelet transfusion, chemotherapy dose reduction, or change in treatment regimen).[14]
- **Immune Thrombocytopenia:** The American Society of Hematology has updated guidelines for ITP (2019). For adults with ITP for at least 3 months who are corticosteroid-dependent or unresponsive to a corticosteroid, a thrombopoietin receptor agonist (Nplate or Promacta® [eltrombopag tablets and oral suspension]) or a splenectomy are recommended.[2] 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.
- **Myelodysplastic Syndrome (MDS):** NCCN recommendations regarding MDS (version 1.2024 – February 12, 2024) 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.

## Medical Necessity Criteria

**Nplate is considered medically necessary when ONE of the following is met:**

**FDA-Approved Indications**

1. **Hematopoietic Syndrome of Acute Radiation Syndrome.** Approve for one dose if the patient has been acutely exposed to myelosuppressive doses of radiation.

   **Dosing.** Approve up to 10 mcg/kg administered subcutaneously given once.

2. **Immune Thrombocytopenia.** Approve if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 3 months if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient meets ONE of the following (a or b):
       - **a)** Patient has a platelet count < 30 x $10^9$/L (< 30,000/mcL); OR
       - **b)** Patient meets BOTH of the following [(1) and (2)]:
         **(1)**Patient has a platelet count < 50 x $10^9$/L (< 50,000/mcL); AND
         **(2)**According to the prescriber the patient is at an increased risk of bleeding; AND
     - **ii.** Patient meets ONE of the following (a or b):
       - **a)** Patient has tried at least one other therapy; OR
         Note: Examples of therapies are systemic corticosteroids, intravenous immunoglobulin, anti-D immunoglobulin, Promacta (eltrombopag tablets and oral suspension), Tavalisse (fostamatinib tablets), Doptelet (avatrombopag tablets), or ritixumab.
       - **b)** Patient has undergone splenectomy; AND
     - **iii.** Medication is prescribed by or in consultation with a hematologist; OR

**B)** Patient is Currently Receiving Nplate. Approve for 1 year if the patient meets BOTH of the following (i and ii):
- **i.** According to the prescriber the patient demonstrates a beneficial clinical response; AND
  Note: A beneficial response can include increased platelet counts, maintenance of platelet counts, and/or a decreased frequency of bleeding episodes.
- **ii.** Patient remains at risk for bleeding complications.

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

**Other Uses with Supportive Evidence**

**3. Thrombocytopenia, Chemotherapy-Induced.** Approve if the patient meets ONE of the following (A or B):

**A)** Initial Therapy. Approve for 3 months if the patient meets ALL of the following (i, ii, iii, and iv):
- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Patient has a platelet count < 100 x $10^9$/L (< 100,000/mcL); AND
- **iii.** Patient meets ONE of the following (a or b):
  - **a)** Patient has thrombocytopenia at least 3 weeks after the most recent dose of chemotherapy; OR
  - **b)** Patient has experienced a delay in chemotherapy administration related to thrombocytopenia; AND
- **iv.** Medication is prescribed by or in consultation with a hematologist or an oncologist; OR

**B)** Patient is Currently Receiving Nplate. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):
- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Patient continues to receive treatment with chemotherapy; AND
- **iii.** Patient demonstrates a beneficial clinical response according to the prescriber.
  Note: A beneficial response can include increased platelet counts, maintenance of platelet counts, and/or decreased frequency of bleeding episodes.

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

**4. Thrombocytopenia in Myelodysplastic Syndrome.** Approve if the patient meets ONE the following (A or B):

**A)** Initial Therapy. Approve for 3 months if the patient meets ALL of the following (i, ii, and iii):
- **i.** Patient has low- to intermediate-risk myelodysplastic syndrome; AND
- **ii.** Patient meets ONE of the following (a or b):
  - **a)** Patient has a platelet count < 30 x $10^9$/L (< 30,000/mcL); OR
  - **b)** Patient meets BOTH of the following [(1) and (2)]:
    - **(1)**Patient has a platelet count < 50 x $10^9$/L (< 50,000/mcL); AND
    - **(2)**According to the prescriber the patient is at an increased risk for bleeding; AND
- **iii.** Medication is prescribed by or in consultation with a hematologist or an oncologist; OR

**B)** Patient is Currently Receiving Nplate. Approve for 1 year if the patient meets BOTH of the following (i and ii):
- **i.** According to the prescriber the patient demonstrates a beneficial clinical response; AND
  Note: A beneficial response can include increased platelet counts, maintenance of platelet counts, and/or decreased frequency of bleeding episodes.
- **ii.** Patient remains at risk for bleeding complications.

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

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

## Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

## References


1. Nplate® subcutaneous injection [prescribing information]. Thousand Oaks, CA: Amgen; February 2022.
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 1.2024 – February 12, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 18, 2024.
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.
6. Sekeres MA, Kantarjian H, Fenaux P, et al. Subcutaneous or intravenous administration of romiplostim in thrombocytopenic patients with lower risk myelodysplastic syndromes. *Cancer*. 2011;117:992-1000.
7. Fenaux P, Muus P, Kantarjian H, et al. Romiplostim monotherapy in thrombocytopenia patients with myelodysplastic syndromes: long-term safety and efficacy. *Br J Haematol*. 2017;178:906-913.
8. Greenberg PL. Garcia-Manero G, Moore M, et al. A randomized controlled trial of romiplostim in patients with low- or intermediate-risk myelodysplastic syndrome receiving decitabine. *Leuk Lymphoma*. 2013;54(2):321-328.
9. Kantarjian H, Fenaux P, Sekeres MA, et al. Safety and efficacy of romiplostim in patients with lower-risk myelodysplastic syndrome and thrombocytopenia. *J Clin Oncol*. 2010;28(3):437-444.
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.
11. Kantarjian HM, Fenaux P, Sekeres MA, et al. Long-term follow-up for up to 5 years on the risk of leukaemic progression in thrombocytopenic patients with lower-risk myelodysplastic syndromes treated with romiplostim or placebo in a randomized double-blind trial. *Lancet Haematol*. 2018;5(3):e117-e126.
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.

14. The NCCN Hematopoietic Growth Factors Clinical Practice Guidelines in Oncology (Version 3.2024 – January 30, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 18, 2024.

## Revision Details

| Type of Revision | Summary of Changes | Date |
|---|---|---|
| Annual Review | **Thrombocytopenia, Chemotherapy-Induced.**<br>**Updated** '(i) Individual has thrombocytopenia at least 2 weeks after the most recent dose of chemotherapy for 2 week cycle regimens, (ii) Individual has thrombocytopenia at least 3 weeks after the most recent dose of chemotherapy for either 3 or 4 week cycle regimens, **TO** (a) Patient has thrombocytopenia at least 3 weeks after the most recent dose of chemotherapy;<br><br>**Thrombocytopenia, Chemotherapy-Induced.**<br>**Updated** reauthorization duration from 1 year to 6 months<br><br>**All covered uses; except Hematopoietic Syndrome of Acute Radiation Syndrome.**<br>**Added** 'Patient is Currently Receiving Nplate'<br><br>**All covered uses.**<br>**Added** dosing<br><br>Title change from Romiplostim. | 8/1/2024 |

The policy effective date is in force until updated or retired.