Clinical Policy: Romiplostim (Nplate)

Reference Number: ERX.SPA.70
Effective Date: 10.01.16
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Romiplostim (Nplate®) is a thrombopoietin receptor agonist.

FDA Approved Indication(s)
Nplate is indicated:

- For the treatment of thrombocytopenia in:
  - Adult patients with immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.
  - 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.
- 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]).

Limitation(s) of use:

- Nplate is not indicated for the treatment of thrombocytopenia due to myelodysplastic syndrome 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.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Nplate is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Hematopoietic Syndrome of Acute Radiation Syndrome (must meet all)**:**

1. Diagnosis of HS-ARS with prescriber attestation that there has been suspected or confirmed exposure to radiation levels greater than 2 gray (Gy);
2. Prescribed by or in consultation with a hematologist;
3. Dose does not exceed 10 mcg/kg.

Approval duration: 4 weeks (1 dose only)

B. Immune Thrombocytopenia (must meet all)**:**

1. Diagnosis of ITP;
2. Prescribed by or in consultation with a hematologist;
3. Age ≥ 1 year;
4. Current (within 30 days) platelet count is < 30,000/µL, or member has an active bleed;
5. Member meets one of the following (a or b):
   a. Failure of a systemic corticosteroid;

b. Member has intolerance or contraindication to systemic corticosteroids, and failure of an immune globulin, unless contraindicated or clinically significant adverse effects are experienced (*see Appendix B*);
**Prior authorization may be required for immunoglobulins*

6. Nplate is not prescribed concurrently with rituximab or another thrombopoietin receptor agonist (e.g., Promacta®, Doptelet®);
7. Dose does not exceed 10 mcg/kg per week.

Approval duration: 6 months

C. Recommended NCCN Uses (off-label) (must meet all)**:**

1. Diagnosis of one of the following (a or b):
   a. Myelodysplastic syndromes (MDS);
   b. Chemotherapy-induced thrombocytopenia (CIT);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. For MDS, member has both of the following (a and b):
   a. Lower-risk MDS (IPSS-R [Very Low, Low, Intermediate]);
   b. Severe or refractory thrombocytopenia following disease progression or no response to hypomethylating agents (e.g., azacitadine, decitabine), immunosuppressive therapy (e.g., Atgam®, cyclosporine), or clinical trial;
4. For CIT, member has platelets < 100,000/ µL for ≥ 3 weeks following the last chemotherapy administration and/or following delays in chemotherapy initiation related to thrombocytopenia
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 10 mcg/kg per week;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

D. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Hematopoietic Syndrome of Acute Radiation Syndrome

1. Re-authorization is not permitted. Members must meet the initial approval criteria.

Approval duration: Not applicable

B. Immune Thrombocytopenia (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy (e.g., increase in platelet count from baseline levels, reduction in bleeding events);
3. Current (within the last 90 days) platelet count is < 400,000/µL;
4. Nplate is not prescribed concurrently with rituximab or another thrombopoietin receptor agonist (e.g., Promacta, Doptelet);
5. If request is for a dose increase, new dose does not exceed 10 mcg/kg per week.

Approval duration: 12 months

C. Recommended NCCN Uses (off-label) (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Nplate for MDS or CIT and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 10 mcg/kg per week;

b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

D. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CIT: chemotherapy-induced thrombocytopenia
FDA: Food and Drug Administration
HS-ARS: hematopoietic syndrome of acute radiation syndrome
IPSS-R: Revised International Prognostic Scoring System
ITP: chronic immune thrombocytopenia
MDS: myelodysplastic syndromes

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Corticosteroids*		
dexamethasone	**ITP** Oral dosage: *Adults*: Initially, 0.75 to 9 mg/day PO, given in 2 to 4 divided doses. Adjust according to patient response *Children and adolescents*: 0.02 to 0.3 mg/kg/day PO or 0.6 to 9 mg/m^2/day PO, given in 3 to 4 divided doses Intramuscular or intravenous dosage: *Adults:* Initially, 0.5 to 9 mg/day IV or IM, given in 2 to 4 divided doses. Adjust according to patient response *Children:* 0.02 to 0.3 mg/kg/day or 0.6 to 9 mg/m^2/day IV or IM given in 3-4 divided doses. Adjust according to patient response	Dosage must be individualized and is highly variable depending on the nature and severity of the disease, route of treatment, and on patient response
methylprednisolone	**ITP** Oral dosage: *Adults:* 4 to 48 mg/day PO in 4 divided doses. Adjust according to patient response. *Children:* 0.5 to 1.7 mg/kg/day PO in divided doses every 6 to 12 hrs Intravenous dosage: *Adults:* 10 to 40 mg IV every 4 to 6 hours for up to 72 hours *Children:* 0.11 to 1.6 mg/kg/day IV in 3 or 4 divided doses.	

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
prednisone	**ITP** *Adults:* Initially, 1 mg/kg PO once daily; however, lower doses of 5 mg/day to 10 mg/day PO are preferable for long-term treatment	
Immune globulins		
immune globulins (Carimune® NF, Flebogamma® DIF 10%, Gammagard® S/D, Gammaked™, Gamunex®-C, Gammaplex®, Octagam® 10%, Privigen®)	Refer to prescribing information	Refer to prescribing information

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Examples of corticosteroids/immunosuppressive agents provided are not all inclusive*

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information
- MDS prognostic scoring system online calculator for IPSS-R: https://qxmd.com/calculate/calculator_109/mds-revised-international-prognostic-scoring-system-ipss-r

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
ITP	The initial dose is 1 mcg/kg SC once weekly based on actual body weight. Adjust weekly dose by increments of 1 mcg/kg to achieve and maintain a platelet count ≥ 50 x 10^9/L as necessary to reduce the risk for bleeding. Do not dose if platelet count is > 400,000/µL.	10 mcg/kg/week
HS-ARS	10 mcg/kg administered once as a SC injection. Administer the dose as soon as possible after suspected or confirmed exposure to myelosuppressive doses of radiation.	10 mcg/kg

VI. Product Availability
Lyophilized powder in single-dose vials for injection: 125 mcg, 250 mcg, 500 mcg

VII. References
1. Nplate Prescribing Information. Thousand Oaks, CA: Amgen Inc.; October 2019. Available at https://www.nplate.com/. Accessed November 15, 2021.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc. Updated periodically. Accessed November 15, 2021.
3. National Comprehensive Cancer Network. Myelodysplastic Syndromes Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed November 15, 2021.
4. National Comprehensive Cancer Network. Hematopoietic Growth Factors Version 4.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/growthfactors.pdf. Accessed November 15, 2021.
5. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November 15, 2021.

6. Christensen DM, Iddins CJ, Parrillo SJ, Glassman ES, and Goans RE. Management of ionizing radiation injuries and illnesses, part 4: acute radiation syndrome. *J Am Osteopath Assoc.* 2014;114: 702-711. doi: 10.7556/jaoa.2014.138.
7. Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Adv (2019) 3 (23): 3829–3866.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q18 annual review: No significant changes. Removed "other causes (e.g., myelodysplastic syndrome) of thrombocytopenia has been ruled out with documentation supporting that ITP is not due to any other causes" since specialist is involved in care.	11.15.17	02.18
Removed requirement related to splenectomy based on specialist feedback.	08.20.18	11.18
1Q 2019 annual review: no significant changes; added requirement that initial platelet counts be current (within 30 days); for cont tx approval, added MDS and other causes of thrombocytopenia other than chronic ITP as diagnoses not covered per package insert; no significant changes; references reviewed and updated.	10.30.18	02.19
1Q 2020 annual review: revised criteria to allow use in non-chronic ITP per revised prescribing information; revised systemic corticosteroid *and* immune globulin trial to tiered re-direction with immune globulin trial only if corticosteroid cannot be used; removed MDS from excluded diagnoses and added criteria set as NCCN supported category 2A recommendation for use; references reviewed and updated.	11.26.19	02.20
Added requirement that Nplate is not prescribed concurrently with rituximab or another thrombopoietin receptor agonist for ITP.	05.19.20	08.20
1Q 2021 annual review: no significant changes; references reviewed and updated.	11.17.20	02.21
1Q 2022 annual review: for MDS removed IPSS and WPSS risk categorizations as IPSS-R is preferred per NCCN; added criteria for HS-ARS indication; added CIT off-label indication per NCCN; references reviewed and updated.	11.15.21	02.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.