Clinical Policy: Romiplostim (Nplate)

Reference Number: CP.PHAR.179
Effective Date: 03.01.16
Last Review Date: 02.22
Line of Business: Commercial, HIM, Medicaid

Coding Implications
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.

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]).

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.

It is the policy of health plans affiliated with Centene Corporation® 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 immune globulins*
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 (i.e., 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 the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy (e.g., increase in platelet count from baseline, 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 Centene benefit, 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 Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CIT: chemotherapy-induced thrombocytopenia
FDA: Food and Drug Administration
Gy: gray
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 for all relevant lines of business 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.	Dosage must be individualized and is highly variable depending on the nature and severity of the disease, route of treatment, and on patient response.
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.	Dosage must be individualized and is highly variable depending on the nature and severity of the disease, route of treatment, and on patient response.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Immune globulins		
immune globulins (Carimune® NF, Flebogamma® DIF 10%, Gammagard® S/D, Gammaked™, Gamunex®-C, Gammaplex®, Octagam® 10%, Privigen®)	**ITP** 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 ≥ 50,000/µL 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.; February 2021. 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. Neunert C, Lim W, Crowther M, et al. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. *Blood.* 2011; 117(16): 4190-4207.
7. 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.
8. Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Adv.* 2019;3(23):3829–3866.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J2796	Injection, romiplostim, 10 mcg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q18 annual review: Policies combined for Centene Medicaid and Commercial lines of business. New policy for Marketplace line of business; No significant changes from previous corporate approved policy; Added age restriction per PI as safety and effectiveness in pediatric patients (< 18 years) have not been established; Commercial: added requirements related to specialist involvement, insufficient response to corticosteroids and immunoglobulins, splenectomy (unless member has contraindications to surgery), and platelet count or active bleed; re-auth: added platelet count < 400 x 10^9/L within the last 90 days; modified initial/continued approval duration from 6 months or to member's renewal period (whichever is longer)/LOB to 6/12 months; Medicaid: 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; References reviewed and updated.	11.15.17	02.18
Removed requirement related to splenectomy based on specialist feedback	08.20.18	11.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2019 annual review: added requirement that initial platelet counts be current (within 30 days); for cont tx approval, clarified that member must be continuing on interferon-based therapy; 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
No significant changes: updated FDA approved indication to include use in children one year of age and older (was previously labeled for adults only)	12.19.18	
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
For immune thrombocytopenia: added requirement that Nplate is not prescribed concurrently with rituximab or other thrombopoietin receptor agonists for ITP.	05.13.20	08.20
1Q 2021 annual review: no significant changes; RT4: added criteria for recently FDA-approved indication, HS-ARS; references to HIM.PHAR.21 revised to HIM.PA.154; 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 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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage

decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.