Clinical Policy Title:	romiplostim
Policy Number:	RxA.239
Drug(s) Applied:	Nplate®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Romiplostim is a thrombopoietin receptor agonist and 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.

Romiplostim is also 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)]. Studies for this indication were not conducted in humans.

Limitation(s) of use:

- Romiplostim is not indicated for the treatment of thrombocytopenia due to myelodysplastic syndrome (MDS) or any cause of thrombocytopenia other than ITP.
- Romiplostim should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increases the risk for bleeding.
- Romiplostim should not be used in an attempt to normalize platelet counts.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
romiplostim (Nplate®)	ITP	The initial dose is 1 mcg/kg SC once weekly based on actual body weight. • In adults, future dose adjustments are based on changes in platelet counts only. • In pediatric patients, future dose adjustments are based on changes in platelet counts and changes in body weight. Reassessment of body weight is recommended every 12 weeks. Adjust weekly dose by increments of 1 mcg/kg to achieve and maintain a platelet count 50×10^9/L or greater as necessary to reduce the risk for bleeding. Do not dose if platelet count is greater than 400×10^9/L. Continue to assess the platelet count weekly. After the platelet count has fallen below 200×10^9 /L, resume at a dose reduced by 1 mcg/kg.	10 mcg/kg/week

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
romiplostim (Nplate®)	HS-ARS	Administer one dose of 10 mcg/kg once subcutaneously. Administer the dose as soon as possible after suspected or confirmed exposure to radiation levels greater than 2 gray (Gy).	10 mcg/kg

Dosage Forms

- Lyophilized powder in single-dose vials for injection: 125 mcg, 250 mcg, 500 mcg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administer by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Chronic Immune Thrombocytopenia (must meet all):

1. Diagnosis of ITP;
2. Prescribed by or in consultation with a hematologist;
3. Member is 1 year of age or older;
4. Current (within 30 days) platelet count is 30×10^9/L or lower or member has an symptomatic bleeding with a platelet count of 50×10^9/L or lower (e.g., significant mucous membrane bleeding, gastrointestinal bleeding);
5. Failure of systemic corticosteroids (at least a 3-month trial) and immunoglobulins, unless contraindicated or clinically significant adverse effects are experienced (*see Appendix B*), or member has had a splenectomy;
   *Prior authorization may be required for immunoglobulins
6. Member is not receiving concomitant thrombopoietin receptor agonists (e.g., avatrombopag, eltrombopag, lusutrombopag) or spleen tyrosine kinase inhibitors (e.g., fostamatinib).
7. Dose does not exceed 10 mcg/kg/week;

Approval Duration
Commercial: 6 months
Medicaid: 6 months

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

1. Diagnosis of HS-ARS;
2. Member is at least 28 days of age or older;
3. Dose does not exceed 10 mcg/kg;

Approval Duration
Commercial: One dose of 10 mcg/kg
Medicaid: One dose of 10 mcg/kg

C. Myelodysplastic Syndromes (off-label use) (must meet all):

1. Diagnosis of lower-to-intermediate risk* MDS;
   * Lower risk defined as IPSS-R (Very Low, Low, Intermediate), IPSS (Low/Intermediate-1), WPSS (Very Low, Low, Intermediate)
2. Prescribed by or in consultation with a hematologist or oncologist;
3. Member has refractory or severe life-threatening thrombocytopenia following disease progression;
4. Failure of therapy with hypomethylating agents (e.g., azacitidine, decitabine), immunosuppressive therapy (e.g., antithymocyte globulin, cyclosporine), or clinical trial;
5. Member is not receiving concomitant thrombopoietin receptor agonists (e.g., avatrombopag, eltrombopag, lusutrombopag) or spleen tyrosine kinase inhibitors (e.g., fostamatinib).
6. Requested dose 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
Commercial: 6 months
Medicaid: 6 months

D. Severe thrombocytopenia Post-Cancer Chemotherapy (off-label use) (must meet all):

1. Diagnosis of chemotherapy-induced thrombocytopenia;
2. Prescribed by or in consultation with a hematologist or oncologist;
3. Platelet count is less than 100×10^9/L for at least 3-4 weeks following last chemotherapy administration and/or following delays in chemotherapy initiation related to thrombocytopenia;
4. Member is not receiving concomitant thrombopoietin receptor agonists (e.g., avatrombopag, eltrombopag, lusutrombopag) or spleen tyrosine kinase inhibitors (e.g., fostamatinib).
5. Requested dose 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
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Chronic Immune Thrombocytopenia (must meet all):

1. Member is currently receiving romiplostim that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
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 less than 400,000/µL;
4. Member is not receiving concomitant thrombopoietin receptor agonists (e.g., avatrombopag, eltrombopag, lusutrombopag) or spleen tyrosine kinase inhibitors (e.g., fostamatinib).
5. If request is for a dose increase, new dose does not exceed 10 mcg/kg/week;

Approval Duration
Commercial: 12 months
Medicaid: 12 months

B. Hematopoietic Syndrome of Acute Radiation Syndrome:
Extension of authorization is not permitted.

C. Myelodysplastic Syndromes (off-label use) (must meet all):
1. Member is currently receiving romiplostim that has been authorized by RxAdvance, or documentation supports that member is currently receiving romiplostim for MDS and has received this medication for at least 30 days;
2. Member is responding positively to therapy (e.g., increase in platelet count);
3. Current (within the last 90 days) platelet count is less than 450,000/µL;
4. Member is not receiving concomitant thrombopoietin receptor agonists (e.g., avatrombopag, eltrombopag, lusutrombopag) or spleen tyrosine kinase inhibitors (e.g., fostamatinib).
5. 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
Commercial: 12 months
Medicaid: 12 months

D. Severe thrombocytopenia Post-Cancer Chemotherapy (off-label use) (must meet all):
1. Member is currently receiving romiplostim that has been authorized by RxAdvance, or documentation supports that member is currently receiving romiplostim for chemotherapy-induced thrombocytopenia and has received this medication for at least 30 days;
2. Member is responding positively to therapy (e.g., increase in platelet count);
3. Current (within the last 90 days) platelet count is less than 150,000/µL;
4. Member is not receiving concomitant thrombopoietin receptor agonists (e.g., avatrombopag, eltrombopag, lusutrombopag) or spleen tyrosine kinase inhibitors (e.g., fostamatinib).
5. 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
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
HS-ARS: Hematopoietic Syndrome of Acute Radiation Syndrome
IPSS: International Prognostic Scoring System
IPSS-R: Revised International Prognostic Scoring System
ITP: Immune thrombocytopenia
MDS: Myelodysplastic Syndromes
NCCN: National Comprehensive Cancer Network
SC: Subcutaneous/SubcutaneouslyWPSS: WHO Classification-based Prognostic Scoring System

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

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*: 0.024 to 0.34 mg/kg/day PO or 0.66 to 10 mg/m^2/day PO, given in 2 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:* 0.06 to 0.3 mg/kg/day or 1.2 to 10 mg/m^2/day IV or IM in divided doses every 6 to 12 hours. 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.

Immune globulins		
immunoglobulins (like 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 provided are not all inclusive.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None
- Boxed Warning(s):
  - None

APPENDIX D: General Information

- MDS prognostic scoring system online calculators are available below:
  - IPSS-R: https://www.mds-foundation.org/ipss-r-calculator/
  - IPSS: https://qxmd.com/calculate/calculator_123/mds-intnl-prognostic-scoring-sysipss
  - WPSS: https://qxmd.com/calculate/calculator_143/mds-who-classification-basedprognostic-scoring-system-wpss
- NCCN guidelines list the use of romiplostim for MDS and chemotherapy-induced thrombocytopenia as a category 2A recommendation.
- The initial dose of romiplostim for MDS is 750 mcg SC weekly. Adjust the dose in 250 mcg increments (from 250 mcg every other week up to 1000 mcg weekly) based on platelet counts. If platelet counts is less than 50×10^9/L for 3 consecutive weeks, increase to the next highest dose level. Withhold romiplostim if platelet count is greater than 450×10^9/L. Dose should be reinitiated when platelet count is less than 200×10^9/L.
- Suggested romiplostim dosing strategy for chemotherapy-induced thrombocytopenia is weekly dosing beginning at 2-4 mcg/kg, increased no more than 1-2 mcg/kg per week to target platelet count of 100×10^9/L to 150×10^9/L. Maximum dose is 10 mcg/kg weekly per prescribing information.

References

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Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1) Clinical policy title and drugs applied were updated 2) Dosage form was updated 3) Dosing regimen updated 4) Continued therapy criteria was updated 5) Diagnosis criteria under initial therapy was updated 6) Added Appendix C 7) Added initial and continued therapy criteria for NCCN category 2A recommendation for use in MDS 8) Appendix B, Abbreviations updated to include MDS, IPSS, WPSS, WHO 9) Added Appendix D, general information 10) Approval duration for initial and continued approval criteria updated to new PA policy format	08/2020	09/14/2020
Policy was reviewed 1) Policy title table was updated. 2) Indications were updated. 3) Dosing regimen was updated. 4) Initial Approval Criteria and Continued Therapy Approval was updated with new indications. 5) Continued therapy criteria II.A.1, II.B.1, II.C.1 was rephrased to “Member is currently receiving medication that has been authorized by RxAdvance..” 6) References were reviewed and updated.	03/25/2021	6/10/2021