09-J0000-88

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Reviewed: 10/08/25

Revised: 06/01/26

Subject: Romiplostim Injection (Nplate™)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT ARSBOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Romiplostim (Nplate™) is an injectable thrombopoietin (TPO) mimetic that increases platelet production by binding and activating the TPO receptor, similar to endogenous TPO. In August 2008, the US Food and Drug Administration (FDA) approved romiplostim for treatment of thrombocytopenia in persons with chronic immune thrombocytopenia purpura (ITP) whose disease was refractory to corticosteroids, immunoglobulins, or splenectomy. It has also been FDA-approved for the treatment of hematopoietic syndrome of acute radiation syndrome (HR-ARS) to increase survival in adults and pediatric patients acutely exposed to myelosuppressive doses of radiation.

ITP is an autoimmune disorder characterized by a destruction of otherwise normal platelets and frequently occurs without a known or identifiable cause; it is considered a diagnosis of exclusion as there are no diagnostic tests to confirm ITP. The American Society of Hematology (ASH) published a guideline outlining the diagnosis and management of ITP. Treatment of newly diagnosed ITP is recommended when the platelet count is less than 30,000. Initial treatment options for ITP include corticosteroids, IVIG, or anti-D.

Persons who are unresponsive to or relapse after initial corticosteroid therapy are considered to have chronic ITP. In this setting, the following treatment options are recommended:

- Splenectomy
- Thrombopoietin receptor agonists (e.g., eltrombopag [Promacta] or romiplostim [Nplate])
- Rituximab (Rituxan)

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines for myelodysplastic syndrome (MDS) support use of romiplostim for severe or refractory thrombocytopenia following disease progression or no response to hypomethylating agents, immunosuppressive therapy, or clinical trial in patients with lower risk disease (low or intermediate-1 category International Prognostic Scoring System (IPSS), Revised International Prognostic Scoring System (IPSS-R) very low, low, or intermediate category, or WHO-classification based prognostic scoring system (WPSS) very low, low, or intermediate category). The NCCN guidelines also provide guidance for the use of romiplostim for chemotherapy-induced thrombocytopenia to maintain the dose schedule and intensity of chemotherapy when the benefit of treatment outweighs the potential risks.

POSITION STATEMENT:

Drug Waste Reduction: Additional medical necessity criteria for dose optimization may apply depending on the requested dose and member's benefit. Refer to Medical Coverage Guideline Drug Waste Reduction, 09-J5000-54.

I. Initiation of romiplostim (Nplate™) **meets the definition of medical necessity** when used to treat **ONE** of the following:

1. Thrombocytopenia associated with chronic immune (idiopathic) thrombocytopenic purpura (ITP) and **ALL** of the following criteria are met:
   A. The member has demonstrated an insufficient response to **EITHER** of the following:
      i. Adequate trial of corticosteroids (e.g., prednisone 1-2 mg/kg for 2-4 weeks)
      ii. Immunoglobulin therapy (e.g., intravenous immune globulin [IVIG])
   B. **ONE** of the following- lab documentation must be submitted:
      i. The member's platelet count is less than 30,000
      ii. The member has symptomatic bleeding or increased risk for bleeding and platelet count is less than 50,000
   C. Romiplostim is not used concurrently with chronic immune globulin therapy, rituximab, fostamatinib (Tavalisse), rilzabrutinib (Wayrilz), or another thrombopoietin receptor agonist (e.g., eltrombopag [Promacta], avatrombopag [Doptelet], lusutrombopag [Mulpleta])
   D. The dose will be initiated between 1 mcg/kg/week and 4 mcg/kg/week and adjusted to platelet response (not to exceed 10 mcg/kg/week); the dose will be provided with a vial size to minimize drug waste
2. Low Risk Myelodysplastic Syndrome (MDS) (i.e., IPSS low and intermediate-1 categories; IPSS-R: Very low, low, intermediate categories; WPSS Very low, low, and intermediate categories) and **ALL** of the following:
   A. **ONE** of the following – lab documentation must be submitted:
      i. The member's platelet count is less than 30,000
      ii. The member has symptomatic bleeding or increased risk for bleeding and platelet count is less than 50,000
   B. The member had an inadequate response or contraindication to a hypomethylating agent (i.e, azacitidine, decitabine)
   C. Romiplostim is not used concurrently with another thrombopoietin receptor agonist (e.g., eltrombopag, avatrombopag, lusutrombopag)
   D. The dose will be initiated between 1 mcg/kg/week and 4 mcg/kg/week and adjusted to platelet response (not to exceed 10 mcg/kg/week); the dose will be provided with a vial size to minimize drug waste
3. Hematopoietic syndrome of acute radiation syndrome (HS-ARS) and **BOTH** of the following:
   A. To increase survival in a member acutely exposed to myelosuppressive doses of radiation
   B. Will be administered as a single dose of 10 mcg/kg
4. Chemotherapy-induced thrombocytopenia (CIT) to maintain dosing schedule and intensity of chemotherapy
   A. The member's platelet count is less than 100,000 for 3 or more weeks following the last chemotherapy administration – lab documentation must be submitted

B. Other potential causes of thrombocytopenia have been ruled out

C. Romiplostim is not used concurrently with another thrombopoietin receptor agonist (e.g., eltrombopag, avatrombopag, lusutrombopag)

D. The dose will be initiated between 1 mcg/kg/week and 4 mcg/kg/week and adjusted to platelet response (not to exceed 10 mcg/kg/week); the dose will be provided with a vial size to minimize drug waste

5. Immune checkpoint inhibitor thrombocytopenia (ICI-T)

A. The member developed thrombocytopenia following the use of an immune-checkpoint inhibitor

B. The member had an inadequate response or contraindication to corticosteroids

C. **ONE** of the following – lab documentation must be submitted:

i. The member's platelet count is less than 50,000

ii. The member's platelet count decreased greater than 50% from baseline

D. Romiplostim is not used concurrently with another thrombopoietin receptor agonist (e.g., eltrombopag, avatrombopag, lusutrombopag)

E. The dose will be initiated between 1 mcg/kg/week and 4 mcg/kg/week and adjusted to platelet response (not to exceed 10 mcg/kg/week); the dose will be provided with a vial size to minimize drug waste

Approval duration: 6 months

II. **Continuation** of romiplostim **meets the definition of medical necessity** when used for the treatment of thrombocytopenia associated with chronic ITP, HS-ARS, low risk MDS, CIT, or ICI-T when **ALL** of the following criteria are met:

A. The member has been previously approved by Florida Blue or another healthplan in the past 2 years for romiplostim for the treatment of chronic ITP, HS-ARS, low risk MDS, CIT, ICI-T **OR** the member previously met all indication-specific criteria

B. The member has a beneficial response to therapy evidenced by an improvement in platelet count from baseline – lab documentation must be submitted

C. Romiplostim is not used concurrently with chronic immune globulin therapy, rituximab, fostamatinib (Tavalisse), rilzabrutinib (Wayrilz) or another thrombopoietin receptor agonist (e.g., eltrombopag, avatrombopag, lusutrombopag)

D. The dose does not exceed 10 mcg/kg in 7 days and will be provided with a vial size to minimize drug waste

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved: romiplostim is indicated for treatment of thrombocytopenia in persons 1 year of age or older with chronic immune thrombocytopenia (ITP) with an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Therapy should only be used in persons with ITP whose degree of thrombocytopenia and clinical condition increases the risk for bleeding; it should not be used in an

attempt to normalize platelet counts. Romiplostim is also indicated to increase survival in adults and pediatric patients (including term neonates) acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome (HS-ARS).

Romiplostim is not indicated for the treatment of thrombocytopenia due to myelodysplastic syndrome or any cause of thrombocytopenia other than chronic ITP.

ITP:

Initial dose: 1 mcg/kg subcutaneously once weekly. The dose should be based on actual body weight.

Dose adjustments: dose adjustments are based on platelet counts. During romiplostim therapy, assess complete blood cell counts (CBCs), including platelet count and peripheral blood smears, weekly until a stable platelet count (50,000 or higher for at least 4 weeks without dose adjustment) has been achieved. Obtain CBCs, including platelet counts and peripheral blood smears, monthly thereafter.

The weekly dose of romiplostim is adjusted in increments of 1 mcg/kg until a platelet count of at least 50,000 as necessary to reduce the risk for bleeding; do not exceed a maximum weekly dose of 10 mcg/kg.

The manufacturer recommends the following dose adjustments based on platelet count:

- If the platelet count is less than 50,000, increase the dose by 1 mcg/kg.
- If platelet count is more than 200,000 for 2 consecutive weeks, reduce the dose by 1 mcg/kg.
- If platelet count is more than 400,000 do not administer. Continue to assess the platelet count weekly. After the platelet count has fallen to less than 200,000, resume romiplostim at a dose reduced by 1 mcg/kg.

Discontinuation: Discontinue romiplostim if the platelet count does not increase to a level sufficient to avoid clinically important bleeding after 4 weeks of romiplostim therapy at the maximum weekly dose of 10 mcg/kg. Obtain CBCs, including platelet counts, weekly for at least 2 weeks following discontinuation of romiplostim.

Maximum dose: 10 mcg/kg weekly.

Acute exposure to myelosuppressive doses of radiation:

10 mcg/kg administered once subcutaneously. The dose should be administered as soon as possible after suspected or confirmed exposure to myelosuppressive doses of radiation.

Drug Availability: romiplostim is supplied as 125-, 250- or 500 mcg single-use vials. See prescribing information for reconstitution instructions.

PRECAUTIONS:

Malignancy: in persons with myelodysplastic syndrome, romiplostim increases blast cell counts and increases the risk of progression to acute myelogenous leukemia.

Coagulopathy: thrombotic/thromboembolic complications may results from increases in platelet counts with romiplostim use. Portal vein thrombosis has been reported in persons with chronic liver disease receiving romiplostim; as such, romiplostim should be used with caution in persons with concomitant ITP and chronic liver disease.

Laboratory monitoring: obtain CBCs, including platelet counts, weekly during the dose-adjustment phase of therapy and then monthly following establishment of a stable dose. Obtain CBCs, including platelet counts, weekly for at least 2 weeks following discontinuation.

Neutralizing antibodies: if severe thrombocytopenia develops during romiplostim treatment, assess for formation of neutralizing antibodies. Hyporesponsiveness or failure to maintain a platelet response may occur due to neutralizing antibodies or other causes.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding:

J2802	Injection, romiplostim, 1 microgram

ICD-10 Diagnosis Codes That Support Medical Necessity:

C93.10	Chronic myelomonocytic leukemia
D46.0	Refractory anemia without ring sideroblasts, so stated
D46.1	Refractory anemia with ring sideroblasts
D46.20 – D46.21	Refractory anemia with excess of blasts
D46.4	Refractory anemia, unspecified
D46.9	Myelodysplastic syndrome, unspecified
D46.A	Refractory cytopenia with multilineage dysplasia
D46.B	Refractory cytopenia with multilineage dysplasia and ring sideroblasts
D46.Z	Other myelodysplastic syndromes
D69.3	Immune thrombocytopenic purpura
T45.1X5A	Poisoning by antineoplastic and immunosuppressive drugs, accidental (unintentional) initial encounter
T45.1X5D	Poisoning by antineoplastic and immunosuppressive drugs, accidental (unintentional) subsequent encounter
T45.1X5S	Poisoning by antineoplastic and immunosuppressive drugs, accidental (unintentional) sequela
T66.XXXA, T66.XXXD, T66.XXXS	Radiation sickness, unspecified

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: No National Coverage Determination (NCD) was found at the time of the last guideline revised date. The following Local Coverage Determination (LCD) was reviewed on the last guideline revised date: Romiplostim (Nplate), (L33748) located at fcso.com.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

International Prognostic Scoring System (IPSS): classification system used in staging individuals with MDS. The IPSS evaluates three components when determining an overall score of 0 to 2.5: percent marrow blasts, cytogenics (e.g., del(5)q chromosome), and cytopenias. An IPSS score of 0 corresponds to low risk, 0.5-1 to intermediate risk 1, 1.5-2 to intermediate risk 2, and 2.5 or greater to high risk.

IPSS Classification System	
Risk Level	IPSS Score
Low risk	0
Intermediate risk 1	0.5-1
Intermediate risk 2	1.5-2
High risk	2.5 or greater

The following factors are used to calculate the IPSS score:

	0	0.5	1.0	1.5	2.0
% Marrow Blasts	Less than 5	5-10		11-20	21-30
Cytogenetics	Normal, -Y, del(5)g alone, del(20)q alone	Other	-7, del (7)q, 3 or more abnormalities		
Cytopenias • Hemoglobin <10 g/dL Neutrophil count less than 1800/mcL • Platelet count less than 100,000 cells/mm3	Only 1	Two of the three			
ANC, absolute neutrophil count					

Myelodysplastic Syndrome (MDS): any of a group of related bone marrow disorders of varying duration preceding the development of overt acute myelogenous leukemia; they are characterized by abnormal hematopoietic stem cells, anemia, neutropenia and thrombocytopenia. Also called releukemia.

Revised International Prognostic Scoring System (IPSS-R): classification system used in staging individuals with MDS. Individuals are assigned to 1 of 5 risk groups.

IPSS-R Classification System	
Risk Level	IPSS-R Score
Very Low	≤1.5
Low	>1.5- ≤3
Intermediate	>3 - ≤4.5
High	>4.5 - ≤6
Very High	>6

The following factors are used to calculate the IPSS-R score

Prognostic variable	0	0.5	1	1.5	2	3	4
Cytogenetics	Very good	-	Good	-	Intermediate	Poor	Very poor
% Marrow Blasts	≤2	-	>2 - <5	-	5-10	>10	-
Hemoglobin	≥10	-	8 - <10	< 8			
Platelets	≥100	50 - <100	<50	-	-	-	-
ANC	≥0.8	<0.8	-	-	-	-	-

ANC, absolute neutrophil count

Thrombocytopenic Purpura: any of various types associated with a decrease in the number of platelets in the blood; there are two general types: in the primary or idiopathic type, the cause is unknown. The secondary or symptomatic type may be associated with exposure to drugs or other chemical agents or with any of numerous different diseases. The most prominent symptoms are bruising and petechiae. In the acute form there may be bleeding from body orifices.

World Health Organization (WHO) Prognostic Scoring System (WPSS): classification system used in staging individuals with MDS. This system is based on the WHO classification of the MDS subtype, karyotype, and presence of severe anemia. Individuals are assigned to 1 of 5 risk groups and the risk category may change over the course of the disease.

WPSS Classification System				
	Score			
Variable	0	1	2	3
WHO Category	RCUD, RARS, MDS with isolated del (5q)	RCMD	RAEB-1	RAEB-2
Karyotype	Good	Intermediate	Poor	--
Severe anemia (hemoglobin <9 g/dL in males or <8 g/dL in females)	Absent	Present	--	--
RCUD, refractory cytopenia with unilineage dysplasia (includes refractory anemia, refractory neutropenia, and refractory thrombocytopenia); RAEB, refractory anemia with excess blasts; RARS, refractory anemia with ringed sideroblasts; RCMD, refractory cytopenia with multilineage dysplasia; A score of 0=very low risk, 1= low risk, 2=intermediate risk, 3-4=high risk, 5-6=very high risk				

RELATED GUIDELINES:

Avatrombopag (Doptelet®), 09-J3000-02
Eltrombopag (Promacta®) Tablets, 09-J1000-13
Fostamatinib (Tavalisse), 09-J3000-00
Immune Globulin Therapy, 09-J0000-06
Lenalidomide (Revlimid®), 09-J0000-80
Oprelvekin; Interleukin 11 (Neumega®), 09-J0000-63
Rituximab (Rituxan), 09-J0000-59

OTHER:

None applicable.

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 10/08/25.

GUIDELINE UPDATE INFORMATION:

03/15/09	New Medical Coverage Guideline.
04/15/09	Revision to guideline; consisting of adding coverage criteria of participation in Nplate™ program and platelet count and listing of non covered indications.
01/01/10	Annual HCPCS coding update: added HCPCS code J2796.
07/15/10	Review and revision to guideline; consisting of adding criteria of 18 years old or older, updated precautions section and updated references.
01/15/11	Revision to guideline; consisting of adding ICD-10 codes.
07/15/11	Review and revision to guideline; consisting of adding maximum dose to coverage criteria and update references.
07/15/12	Review and revision to guideline; consisting of updating position statement, precautions, program exceptions and references.
07/15/13	Review and revision to guideline; consisting of revising position statement to include recommendations from current American Society of Hematology guidelines for treatment of ITP, reformatting and revising description, dosage/administration, program exceptions and precautions section; updating references.
07/15/14	Review and revision to guideline; consisting of revising position statement and updating references.
07/15/15	Review and revision to guideline; consisting of updating precautions and references.
10/01/15	Revision consisting of update to Program Exceptions section.
10/15/15	Revision to guideline; consisting of updated position statement.
11/01/15	Revision: ICD-9 Codes deleted.
07/15/16	Review and revision to guideline; consisting of updating position statement, description, and references.
12/15/19	Review and revision to guideline; consisting of updating position statement and references.
12/15/20	Revision to guideline; consisting of updating the description and references.
08/15/21	Revision to guideline; consisting of updating the position statement, description, dosing, coding and references.
12/15/22	Review and revision to guideline; consisting of updating documentation of platelet improvement under continuation criteria and updating references.

12/15/23	Revision to guideline; consisting of updating the position statement and references.
01/01/25	Revision: Added HCPCS code J2802 and deleted code J2796.
11/15/25	Review and revision to guideline; consisting of including immune-checkpoint inhibitor thrombocytopenia into the position statement.
06/01/26	Revision: Added Drug Waste Reduction statement to the Position Statement.