

Coverage of any drug intervention discussed in the plans prior authorization guideline is subject to the limitations and exclusions outlined in the member's benefit certificate or policy and to applicable state and/or federal laws.

Nplate[®] (romiplostim) (Subcutaneous)

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Effective Date: 01/01/2023

I. Length of Authorization

Coverage will be provided for 3 months and may be renewed, unless otherwise specified.

- Coverage for use to treat Hematopoietic Syndrome of Acute Radiation Syndrome (HS-ARS) cannot be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Nplate 125 mcg single-dose vial for injection: 40 vials per 28 days
- Nplate 250 mcg single-dose vial for injection: 20 vials per 28 days
- Nplate 500 mcg single-dose vial for injection: 12 vials per 28 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- ITP and CIT: 125 billable units weekly
- MDS: 100 billable units weekly
- HS-ARS: 125 billable units x 1 dose

III. Initial Approval Criteria ¹

Coverage is provided in the following conditions:

Universal Criteria ¹

- Patient is not on any other thrombopoietin receptor agonist or mimetic (e.g., lusutrombopag, eltrombopag, avatrombopag, etc.) or fostamatinib; **AND**
- Romiplostim is not being used to attempt to normalize platelet count; **AND**

- Laboratory values for platelet count are current (i.e., drawn within the previous 28 days); **AND**

Immune (idiopathic) thrombocytopenia (ITP) † Φ^{1,5}

- The patient is at increased risk for bleeding as indicated by platelet count less than $30 \times 10^9/L$ ($30,000/mm^3$); **AND**
 - Patient has acute ITP; **AND**
 - Patient is at least 18 years of age; **AND**
 - Patient has previously failed any of the following treatments for ITP:
 - Patient has failed previous therapy with corticosteroids; **OR**
 - Patient has failed previous therapy with immunoglobulins; **OR**
 - Patient has had a splenectomy; **OR**
 - Patient has had chronic ITP for at least 6 months (or meets the corticosteroid requirement below); **AND**
 - Patient is at least 1 year of age; **AND**
 - Patient has previously failed any of the following treatments for ITP:
 - Patient has failed previous therapy with corticosteroids (i.e., patient had no response to at least a 3-month trial or is corticosteroid-dependent); **OR**
 - Patient has failed previous therapy with immunoglobulins; **OR**
 - Patient has had a splenectomy

Hematopoietic Syndrome of Acute Radiation Syndrome (HS-ARS) † Φ¹

- Patient has suspected or confirmed exposure to radiation levels greater than 2 gray (Gy)

Chemotherapy-Induced Thrombocytopenia (CIT) ‡^{2,16-18}

- Patient is at least 18 years of age; **AND**
- Patient has a platelet count less than $100 \times 10^9/L$ ($100,000/mm^3$) for at least 3 to 4 weeks after the last chemotherapy administration and/or after delays on chemotherapy initiation related to thrombocytopenia

Myelodysplastic Syndromes (MDS) ‡^{2,3,13,14}

- Patient is at least 18 years of age; **AND**
- Patient has lower risk disease [i.e., IPSS-R (Very Low, Low, Intermediate)]; **AND**
- Patient has severe or refractory thrombocytopenia (i.e., platelet count $<20 \times 10^9/L$ or higher with a history of bleeding); **AND**
- Patient progressed or had no response to hypomethylating agents (e.g., azacitidine, decitabine, etc.), immunosuppressive therapy, or clinical trial

† FDA-labeled indication(s); ‡ Compendia recommended indication(s); Ⓟ Orphan Drug

IV. Renewal Criteria ¹

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: thrombotic/thromboembolic complications, risk of progression of myelodysplastic syndromes to acute myelogenous leukemia, etc.; **AND**

Immune (idiopathic) thrombocytopenia (ITP) ¹

- Disease response indicated by the achievement and maintenance of a platelet count of at least $50 \times 10^9/L$ (not to exceed $400 \times 10^9/L$) as necessary to reduce the risk for bleeding

Hematopoietic Syndrome of Acute Radiation Syndrome (HS-ARS) ¹

- Coverage cannot be renewed

Chemotherapy-Induced Thrombocytopenia (CIT) ^{2,15-18}

- Patient continues to receive chemotherapy; **AND**
- Disease response indicated by the achievement and maintenance of a platelet count of at least $100 \times 10^9/L$ (not to exceed $400 \times 10^9/L$)

Myelodysplastic Syndromes (MDS) ^{2,3}

- Patient has not developed acute myeloid leukemia (AML) (Note: romiplostim induces an increase in immature white blood cells and peripheral blasts which is not indicative of development of AML); **AND**
- Disease response indicated by an increase in platelet count compared to pretreatment baseline (not to exceed $450 \times 10^9/L$), reduction in bleeding events, or reduction in platelet transfusion requirements

V. Dosage/Administration ¹⁻³

Indication	Dose
ITP	<p><u>ADULT/PEDIATRIC</u></p> <p><u>Initial</u>: 1 mcg/kg subcutaneously weekly</p> <ul style="list-style-type: none"> • Adjust dose weekly by increments of 1 mcg/kg to achieve and maintain platelet count of $\geq 50 \times 10^9/L$ ($50,000/mm^3$) as necessary to reduce the risk for bleeding • Do not exceed the maximum weekly dose of 10 mcg/kg • Adjust the dose as follows for all patients:

Indication	Dose
	<ul style="list-style-type: none"> – If the platelet count is $< 50 \times 10^9/L$, increase the dose by 1 mcg/kg. – If platelet count is $> 200 \times 10^9/L$ and $\leq 400 \times 10^9/L$ for 2 consecutive weeks, reduce the dose by 1 mcg/kg. – If platelet count is $> 400 \times 10^9/L$, do not dose. Continue to assess the platelet count weekly. After the platelet count has fallen to $< 200 \times 10^9/L$, resume Nplate at a dose reduced by 1 mcg/kg.
HS-ARS	<u>ADULT/PEDIATRIC</u> 10 mcg/kg subcutaneously x 1 dose administered as soon as possible after suspected or confirmed exposure to radiation.
CIT	<u>Initial:</u> 2 to 4 mcg/kg weekly <ul style="list-style-type: none"> • Increase by no more than 1 to 2 mcg/kg per week to target platelet count of $100 \times 10^9/L$ to $150 \times 10^9/L$. • Do not exceed the maximum weekly dose of 10 mcg/kg.
MDS	<u>Initial:</u> 750 mcg weekly <ul style="list-style-type: none"> • Adjust dose in 250 mcg increments (from 250 mcg every other week up to 1000 mcg weekly) based on platelet counts <ul style="list-style-type: none"> ○ If platelet count is $<50 \times 10^9/L$ for 3 consecutive weeks, then increase to the next highest dose level • Withhold the dose if platelet count $>450 \times 10^9/L$ <ul style="list-style-type: none"> ○ Reinitiate at a reduced dose when platelet count is $<200 \times 10^9/L$

VI. Billing Code/Availability Information

HCPCS Code:

- J2796 – Injection, romiplostim, 10 micrograms; 10 mcg = 1 billable unit

NDC(s):

- Nplate 125 mcg single-dose vial: 55513-0223-xx
- Nplate 250 mcg single-dose vial: 55513-0221-xx
- Nplate 500 mcg single-dose vial: 55513-0222-xx

VII. References

1. Nplate [package insert]. Thousand Oaks, CA; Amgen Inc; February 2021. Accessed January 2022.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for romiplostim. National Comprehensive Cancer Network, 2022. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to www.nccn.org/. Accessed January 2022.

3. 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 Jun 15;120(12):1838-46.
4. Lambert MP, Gernsheimer TB. Clinical updates in adult immune thrombocytopenia. *Blood*. 2017. 129:2829-2835. Doi:10.1182/blood-2017-03-754119.
5. Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Adv*. 2019 Dec 10;3(23):3829-3866.
6. Newland A, Godeau B, Priego V, et al. Remission and platelet responses with romiplostim in primary immune thrombocytopenia: final results from a phase 2 study. *Br J Haematol*. 2016 Jan;172(2):262-73. Doi: 10.1111/bjh.13827.
7. Bussel JB, Buchanan GR, Nugent DJ, et al, "A Randomized, Double-Blind Study of Romiplostim to Determine Its Safety and Efficacy in Children With Immune Thrombocytopenia," *Blood*, 2011, 118(1):28-36.
8. Bussel JB, Kuter DJ, Pullarkat V, et al, "Safety and Efficacy of Long-Term Treatment With Romiplostim in Thrombocytopenic Patients With Chronic ITP," *Blood*, 2009, 113(10):2161-71.
9. Kuter DJ, Bussel JB, Lyons RM, et al, "Efficacy of Romiplostim in Patients With Chronic Immune Thrombocytopenic Purpura: A Double-Blind Randomised Controlled Trial," *Lancet*, 2008, 371(9610):395-403.
10. Kuter DJ, Rummel M, Boccia R, et al, "Romiplostim or Standard of Care in Patients With Immune Thrombocytopenia," *N Engl J Med*, 2010, 363(20):1889-99.
11. Kuter DJ, Bussel JB, Newland A, et al. Long-term treatment with romiplostim in patients with chronic immune thrombocytopenia: safety and efficacy. *Br J Haematol*. 2013 May;161(3):411-23. Doi: 10.1111/bjh.12260.
12. Tarantino MD, Bussel JB, Blanchette VS, et al. Romiplostim in children with immune thrombocytopenia: a phase 3, randomised, double-blind, placebo-controlled study. *Lancet*. 2016 Jul 2;388(10039):45-54. Doi: 10.1016/S0140-6736(16)00279-8.
13. 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 Jan 20;28(3):437-44.
14. 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 Oct 28;116(17):3163-70.
15. Soff GA, Miao Y, Bendheim G, et al. Romiplostim Treatment of Chemotherapy-Induced Thrombocytopenia. *J Clin Oncol*. 2019 Nov 1;37(31):2892-2898. doi: 10.1200/JCO.18.01931.
16. Al-Samkari H, Parnes AD, Goodarzi K, et al. A multicenter study of romiplostim for chemotherapy-induced thrombocytopenia in solid tumors and hematologic malignancies. *Haematologica*. 2021 Apr 1;106(4):1148-1157. doi: 10.3324/haematol.2020.251900.
17. Miao J, Leblebjian H, Scullion B, et al. A single center experience with romiplostim for the management of chemotherapy-induced thrombocytopenia. *Am J Hematol*. 2018 Aug;93(4):E86-E88. doi: 10.1002/ajh.25022.

18. Parameswaran R, Lunning M, Mantha S, et al. Romiplostim for management of chemotherapy-induced thrombocytopenia. Support Care Cancer. 2014 May;22(5):1217-22. doi: 10.1007/s00520-013-2074-2.
19. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hematopoietic Growth Factors 1.2022. National Comprehensive Cancer Network, 2022. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc.” To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed January 2022.
20. CGS Administrators, LLC. Local Coverage Article: Billing and Coding: Immune Thrombocytopenia (ITP) Therapy (A57160). Centers for Medicare & Medicaid Services, Inc. Updated on 02/24/2021 with effective date 03/04/2021. Accessed January 2022.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C93.10	Chronic myelomonocytic leukemia not having achieved remission
D46.0	Refractory anemia without ring sideroblasts, so stated
D46.1	Refractory anemia with ring sideroblasts
D46.20	Refractory anemia with excess of blasts, unspecified
D46.21	Refractory anemia with excess of blasts 1
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
D69.5	Secondary thrombocytopenia
D69.6	Thrombocytopenia, unspecified
T45.1X5A	Adverse effect of antineoplastic and immunosuppressive drugs, initial encounter
T45.1X5D	Adverse effect of antineoplastic and immunosuppressive drugs, subsequent encounter
T45.1X5S	Adverse effect of antineoplastic and immunosuppressive drugs, sequela
T66	Radiation sickness, unspecified

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles may exist and compliance with these policies is required where applicable. They can be found at:

<https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA):

Jurisdiction(s): 15	NCD/LCD/Article Document (s): A57160
https://www.cms.gov/medicare-coverage-database/new-search/search-results.aspx?keyword=a57160&areaId=all&docType=NCA%2CCAL%2CNCD%2CMEDCAC%2CTA%2CMD%2C6%2C3%2C5%2C1%2CF%2CP	

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC