**Approved Revision: Do Not Implement Until 6/2/21**

# Romiplostim (Nplate®)

**NDC CODE(S)** 55513-0221-XX NPLATE 250MCG Solution Reconstituted (AMGEN)
55513-0222-XX NPLATE 500MCG Solution Reconstituted (AMGEN)
55513-0223-XX NPLATE 125MCG Solution Reconstituted (AMGEN)

## DESCRIPTION

Romiplostim is an Fc-peptide fusion protein of the TPO mimetic class and is considered a thrombopoietin receptor agonist. It is produced by recombinant DNA technology in *Escherichia coli (E. coli)*. Through binding and activation of the TPO receptor, romiplostim increases platelet production in the same way that endogenous TPO functions in the body. Increases in platelet counts are romiplostim dose-dependent.

## POLICY

- Romiplostim for the treatment of thrombocytopenia is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
- Romiplostim for the treatment of other conditions/diseases is considered ***investigational.***

## MEDICAL APPROPRIATENESS

### INITIAL APPROVAL CRITERIA

#### Universal Criteria

- Patient is not on any other thrombopoietin receptor agonist or mimetic (e.g., lusutrombopag, eltrombopag, avatrombopag, etc.) or fostamatinib; **AND**
- Must not be used in an attempt to normalize platelet counts; **AND**
- Laboratory value for platelet count is current (i.e., drawn within the previous 28 days); **AND**

#### Immune (idiopathic) thrombocytopenia (ITP)

- The patient is at increased risk for bleeding as indicated by platelet count less than 30 × 109/L (30,000/mm³); **AND**
  - Patient has acute ITP; **AND**
    - Patient is at least 18 years of age; **AND**
    - Patient has previously failed one 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 with chronic ITP for at least 6 months (or meets the corticosteroid requirement below); **AND**
    - Patient is 1 year of age or older; **AND**
    - Patient has previously failed one 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)

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

**Myelodysplastic Syndromes (MDS)**

- Patient is at least 18 years of age; **AND**
- Patient has lower risk disease [i.e., IPSS-R (Very Low, Low, Intermediate), IPSS (Low/Intermediate-1), WPSS (Very Low, Low, Intermediate)]; **AND**
- Patient has severe or refractory thrombocytopenia (i.e., platelet count <20 x 109/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

**RENEWAL CRITERIA**

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

**ITP**

- Disease response indicated by the achievement and maintenance of a platelet count of at least 50 × 109/L (not to exceed 400 x 109/L) as necessary to reduce the risk for bleeding

**HS-ARS**

- Coverage cannot be renewed

**MDS**

- 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 x 109/L), reduction in bleeding events, or reduction in platelet transfusion requirements

**DOSAGE/ADMINISTRATION**

| INDICATION | DOSE |
|---|---|
| ITP | ADULT/PEDIATRIC<br>Initial: 1 mcg/kg subcutaneously weekly<br>• Adjust dose weekly by increments of 1 mcg/kg to achieve and maintain platelet count of ≥ 50 × 109/L (50,000/mm³) as necessary to reduce the risk for bleeding<br>• Do not exceed the maximum weekly dose of 10 mcg/kg<br>• Adjust the dose as follows for all patients:<br>○ If the platelet count is < 50 × 109/L, increase the dose by 1 mcg/kg.<br>○ If platelet count is > 200 × 109/L and ≤ 400 × 109/L for 2 consecutive weeks, reduce the dose by 1 mcg/kg.<br>○ If platelet count is > 400 × 109/L, do not dose. Continue to assess the platelet count weekly. After the platelet count has fallen to < 200 × 109/L, resume Nplate at a dose reduced by 1 mcg/kg. |

| | |
|---|---|
| Hematopoietic Syndrome of Acute Radiation Syndrome | ADULT/PEDIATRIC<br>• 10 mcg/kg subcutaneously x 1 dose administered as soon as possible after suspected or confirmed exposure to radiation |
| MDS | Initial: 750 mcg weekly<br>• Adjust dose in 250 mcg increments (from 250 mcg every other week up to 1000 mcg weekly) based on platelet counts<br>○ If platelet count is <50 x $10^9$/L for 3 consecutive weeks, then increase to the next highest dose level<br>○ Withhold the dose if platelet count >450 x $10^9$/L<br>○ Reinitiate at a reduced dose when platelet count is <200 x $10^9$/L |

**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 (HSARS) cannot be renewed.

**DOSING LIMITS**

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

- TP: 125 billable units weekly
- MDS: 75100 billable units weekly
- HSARS: 125 billable units x 1 dose

**APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS**

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

**IMPORTANT REMINDER**

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

**ADDITIONAL INFORMATION**

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

**SOURCES**

1. Nplate [package insert]. Thousand Oaks, CA; Amgen Inc; January 2021. Accessed January 2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for romiplostim. National Comprehensive Cancer Network, 20201. 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 2021.
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. Lexi-Comp Online. (2021). AHFS DI. *Romiplostim*. Retrieved February 11, 2021 from Lexi Comp Online with AHFS.
16. MICROMEDEX Healthcare Series. Drugdex Evaluations. (2021, February). *Romiplostim*. Retrieved February 11, 2021 from MICROMEDEX Healthcare Series.

**EFFECTIVE DATE** 6/2/2021

ID_MRx