WellMed Doctors helping patients for more than 25 years	**Effective Date:** 08/18/2022	**Revision Date(s):** 04/09/2020, 05/13/2021, 06/16/22
Department: PHARMACY	**MMC Review/ Approval Date(s):** 11/13/18, 5/12/2020, 5/25/2021, 08/09/22	**Total Page(s): 10**

Policy Number & Title: 006.003

Coverage Determination Policy for Romiplostim (Nplate®)

Regions: ☒ **Texas** ☐ **Florida** ☐ **New Jersey** ☒ **New Mexico**

Impacted Areas:

- ☒ Network Management/Provider Services
- ☐ Member services
- ☐ Quality Management
- ☐ Credentialing
- ☐ IT
- ☐ Administration
- ☐ Compliance/delegation
- ☒ Utilization Management
- ☐ Case management
- ☐ Disease management
- ☒ Claims
- ☐ Human resources
- ☐ Finance
- ☒ Pharmacy
- ☐ ALL

Available LCD/NCD/LCA: None for regions above

WellMed Coverage Determination Policies are developed as needed, are regularly reviewed and updated, and are subject to change. They represent a portion of the resources used to support WellMed coverage decision making. WellMed may modify these Policy Guidelines at any time. Medicare source materials used to develop these guidelines include, but are not limited to, CMS National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Medicare Benefit Policy Manual, Medicare Claims Processing Manual, Medicare Program Integrity Manual, Medicare Managed Care Manual, etc. The information presented in the WellMed Coverage Determination Policies is believed to be accurate and current as of the date of publication, and is provided on an "AS IS" basis. Where there is a conflict between this document and Medicare source materials, the Medicare source materials will apply.

WELLMED
Doctors helping patients for more than 25 years

Title: Coverage Determination Policy for Romiplostim (Nplate®)

Coverage Policy Number: 006.003
Line of Business: Medicare Part B
Policy Type: Prior Authorization

Table of Contents **Page**

Initial Requests

- **WellMed will cover romiplostim (Nplate®) as medically necessary for Immune thrombocytopenia (ITP) when ALL of the following criteria are met:**

  - Patient has been diagnosed with chronic ITP
  - Patient has insufficient response or contraindications to one of the following first line therapies: corticosteroids immunoglobulins or splenectomy

Table 3. Definitions of response to treatment by ITP*

Complete response (CR)	A platelet count ≥ 100 × 10^9/L measured on 2 occasions > 7 days apart and the absence of bleeding.
Response (R)	A platelet count ≥ 30 × 10^9/L and a greater than 2-fold increase in platelet count from baseline measured on 2 occasions > 7 days apart and the absence of bleeding.
No response (NR)	A platelet count < 30 × 10^9/L or a less than 2-fold increase in platelet count from baseline or the presence of bleeding. Platelet count must be measured on 2 occasions more than a day apart.
Loss of complete response	A platelet count < 100 × 10^9/L measured on 2 occasions more than a day apart and/or the presence of bleeding.
Loss of response	A platelet count < 30 × 10^9/L or a less than 2-fold increase in platelet count from baseline or the presence of bleeding. Platelet count must be measured on 2 occasions more than a day apart.

*Based on the recommendations of the International Working Group.[7]

Dosing regimen and dose titration is consistent with FDA-approved labeling (see Approved Dosing)

- **WellMed will cover romiplostim (Nplate®) as medically necessary for Hematopoietic subsyndrome of acute radiation syndrome when ALL of the following criteria are met:**
    - Patient has suspected or confirmed exposure to radiation levels greater than 2 gray (Gy)
    - Dosing regimen is consistent with FDA-approved labeling (see FDA Authorization Dosing)

Renewal/Continuation of Therapy

- **WellMed will cover romiplostim (Nplate®) as medically necessary for Immune thrombocytopenia when ALL of the following criteria are met:**
    - Platelet count is NOT > 400 x 10^9/L

      Documentation of positive clinical response
    - CBC monitored according to FDA labeling. Should be monitored weekly during dose adjustments then monthly after dose establishment.
    - Dosing regimen and dose titration remains consistent with FDA-approved labeling **(see FDA Authorization Dosing**)
    - Dose does not exceed MAX dose of 10mcg/kg weekly

- **WellMed will cover romiplostim (Nplate®) as medically necessary for Hematopoietic subsyndrome of acute radiation syndrome when ALL of the following criteria are met:**
  - Documentation of positive clinical response
  - Dosing is consistent with FDA Authorization Dosing (see below)

- **Limitations of Use:**
  - Nplate should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increases the risk for bleeding.
  - Nplate is not indicated for the treatment of thrombocytopenia due to MDS or any cause of thrombocytopenia other than persistent ITP
  - Nplate should not be used in an attempt to normalize platelet counts

FDA Authorization Dosing:

Immune thrombocytopenia

- Initial Dosage:
  - 1mcg/kg (actual body weight) SQ once weekly
- Dose Adjustments:
  - Titrate weekly in increments per the Package Insert below using the lowest dose possible to achieve and maintain a platelet count greater than or equal to 50 x 10(9)/L:

Platelet Count	Dose Adjustment or Response
Less than 50 x 10(9)/L	Increase weekly dose by 1 mcg/kg (MAX 10 mcg/kg/week).
Greater than 200 x 10(9)/L for 2 consecutive weeks	Reduce the weekly dose by 1 mcg/kg
Greater than 400 x 10(9)/L	Discontinue romiplostim. Assess platelet counts weekly.
	When platelet count is less than 200 x 10(9)/L, reinitiate therapy at a weekly dose reduced by 1 mcg/kg.

- **MAXIMUM** weekly dose: 10 mcg/kg
- **Discontinuation:**
  - Discontinue Nplate if the platelet count does not increase to a level sufficient to avoid clinically important bleeding after 4 weeks at the MAX dose.

- NOTE: Obtain CBCs, including platelet counts, weekly for at least 2 weeks following discontinuation of romiplostim
- Dose Adjustments:
  - 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.

Hematopoietic subsyndrome of acute radiation syndrome

- 10 mcg/kg subQ single injection administered as soon as possible after suspected or confirmed exposure to radiation levels greater than 2 gray (Gy). Administer regardless of whether a CBC can be obtained. Estimate the whole-body absorbed dose based on information from public health

authorities, biodosimetry if available, or clinical findings (e.g., time to onset of vomiting or lymphocyte depletion kinetics)

Background:

The disease and its most widely accepted abbreviation, ITP, has variably been defined as "immune thrombocytopenic purpura," "idiopathic thrombocytopenic purpura," and, most recently, "immune thrombocytopenia." It is an autoimmune disorder characterized by immunologic destruction of otherwise normal platelets most commonly occurring in response to an unknown stimulus. ITP may occur in isolation (primary) or in association with other disorders (secondary). Secondary causes include autoimmune diseases (particularly the antiphospholipid antibody syndrome), viral infections (including hepatitis C [HCV] and human immunodeficiency virus [HIV]), and certain drugs. Historically, ITP was believed to be caused by increased platelet destruction at a rate that exceeded production by a compensating bone marrow. New knowledge has questioned this model, providing evidence that platelet production is also decreased in many patients with ITP.

Per the ASH 2019 Evidence Based Practice Guideline for ITP: primary ITP was defined by the IWG as a platelet count less than 100 $X10^9$/L in the absence of other causes or disorders that may be associated with thrombocytopenia. The IWG based its recommendations for the use of an upper-threshold platelet count of 100 X 10^9/L on 3 considerations: a study demonstrating that patients presenting with a platelet count between 100 and 150 X 10^9/L have only a 6.9% chance of developing a persistent platelet count of less than 100 X 10^9/L over 10 years of follow-up; recognition that in non-Western ethnicities normal values in healthy individuals may be between 100 and 150 X 10^9/L. The IWG also defines ITP as newly diagnosed (diagnosis to 3 months), persistent (3 to 12 months from diagnosis), or chronic (lasting for more than 12 months). For the Guideline the IWG used the definitions of ITP used by the authors of the contributing papers and the diagnostic threshold(s) established in their inclusion and exclusion criteria (usually less than 150 X 10^9/L).

Nplate® is a thrombopoietin receptor agonist indicated for the treatment of thrombocytopenia in patients with persistent immune thrombocytopenia (ITP) whom had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.

Nplate® is indicated in 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.

The most common adverse reactions (≥ 5% higher patient incidence in Nplate versus placebo) are arthralgia, dizziness, insomnia, myalgia, pain in extremity, abdominal pain, shoulder pain, dyspepsia, and paresthesia. Headache was the most commonly reported adverse reaction that did not occur at ≥ 5% higher patient incidence in Nplate versus placebo. There are no specific contraindications; however, caution should be used in patients failing to respond or maintaining a response or patients with hepatic impairment.

Romiplostim is indicated to increase survival in adult and pediatric patients (including term neonates) acutely exposed to myelosuppressive doses of radiation. Efficacy studies in humans with acute radiation syndrome were not conducted. Recommendations for use are based on efficacy studies in animals, romiplostim's effect on platelet count in healthy human volunteers, and on data supporting romiplostim's effect on thrombocytopenia in patients with ITP and insufficient response to corticosteroids, immunoglobulins, or splenectomy; safety was based on the latter 2 populations

There are no NCDs or relevant Texas LCDs for Nplate® available at the time of this policy creation.

NOTE: Antibody development has been reported; if suspected, contact Amgen (1-800-772-6436) for assays to detect neutralizing antibodies to romiplostim and thrombopoietin

NCCN Recommended Use of Romiplostim (category 2A) in the Management of Thrombocytopenia:

Patients should be evaluated and treated accordingly for other potential causes of thrombocytopenia.

Suspected chemotherapy-induced thrombocytopenia (CIT):

- **There is currently no FDA-approved treatment for CIT[9]**
- Definitions used in several studies include thrombocytopenia (platelets < 100,000/mcL) for ≥3-4 weeks following last chemotherapy administration and/or following delays in chemotherapy initiation related to thrombocytopenia[9].
- The primary purpose of TPO-RAs for CIT is to maintain dose schedule and intensity of chemotherapy when such benefit is thought to outweigh potential risks[9].
- Beginning dose: 2-4 mcg/kg weekly, increased no more than 1-2 mcg/kg per week to target platelet count (100,000 – 150,000/mcL). Maximum dose is 10 mcg/kg weekly per prescribing information.

Coding Information:

HCPCS Code: Injection, Romiplostim, 10 mcg – J2796

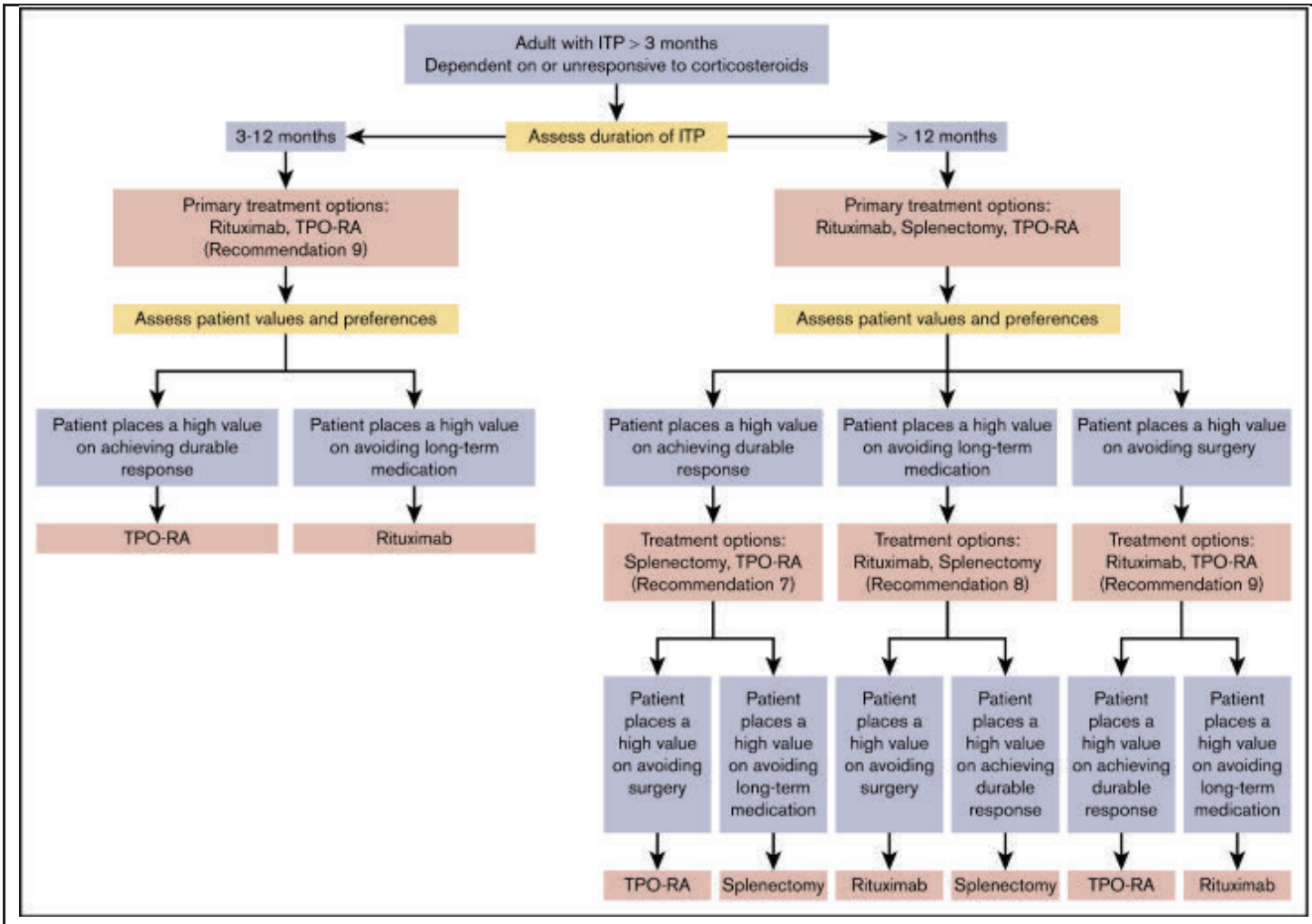
Acronyms:

ITP = Immune Thrombocytopenia Purpura, MDS = myelodysplastic syndrome, IWG = International Working Group, HCV = Hepatitis C virus, HIV = human immunodeficiency virus, MDS = myelodysplastic syndrome; ASH = American Society of Hematology, TPO-RA= Thrombopoietin receptor agonist, Chemotherapy-induced thrombocytopenia (CIT)

Clinical Evidence/Professional Guidelines:

The ASH 2019 Evidence-based Practice Guideline for Immune Thrombocytopenia

These guidelines focus on the management of immune thrombocytopenia (ITP). ITP is an acquired autoimmune disorder characterized by a low platelet count resulting from platelet destruction and impaired platelet production.
The purpose of these guidelines is to provide evidence-based recommendations for the management of adults and children with ITP. The primary goals of these guidelines are to review, critically appraise, and implement evidence-based recommendations that describe the impact of treatments, platelet count response, adverse events, and patient-reported outcomes. Through improved provider and patient education of the available evidence and evidence-based recommendations, this guideline aims to provide clinical decision-making support for different treatment pathways.



Algorithm for the selection of second-line therapy in adults with ITP. Selection of second-line therapy in adults with ITP should be individualized based on duration of disease and patient values and preferences. Other factors that may influence treatment decisions include frequency of bleeding sufficient to require hospitalization or rescue medication, comorbidities, compliance, medical and social support networks, cost, and availability of treatments. Patient education and shared decision-making is encouraged. Patient characteristics are shown in blue boxes, actions in yellow boxes, and treatment options in red boxes. Numbered recommendations corresponding to each treatment option are provided.

Recommendation 1a
In adults with newly diagnosed ITP and a platelet count of $<30 \times 10^9$/L who are asymptomatic or have minor mucocutaneous bleeding, the ASH guideline panel suggests corticosteroids rather than management with observation

Recommendation 1b
In adults with newly diagnosed ITP and a platelet count of $\geq 30 \times 10^9$/L who are asymptomatic or have minor mucocutaneous bleeding, the ASH guideline panel recommends against corticosteroids and in favor of management with observation

Recommendation 2a

In adults with newly diagnosed ITP and a platelet count of <20 × 10^9/L who are asymptomatic or have minor mucocutaneous bleeding, the ASH guideline panel suggests admission to the hospital rather than management as an outpatient

Recommendation 2b
In adults with a platelet count of ≥20 × 10^9/L who are asymptomatic or have minor mucocutaneous bleeding, the ASH guideline panel suggests outpatient management rather than hospital admission

Recommendation 3
In adults with newly diagnosed ITP, the ASH guideline panel recommends against a prolonged course (>6 weeks including treatment and taper) of prednisone and in favor of a short course (≤6 weeks)

Recommendation 4
In adults with newly diagnosed ITP, the ASH guideline panel suggests either prednisone (0.5-2.0 mg/kg per day) or dexamethasone (40 mg per day for 4 days) as the type of corticosteroid for initial therapy

Recommendation 5
In adults with newly diagnosed ITP, the ASH guideline panel suggests corticosteroids alone rather than rituximab and corticosteroids for initial therapy

Recommendation 6
In adults with ITP for ≥3 months who are corticosteroid-dependent or unresponsive to corticosteroids and are going to be treated with a TPO-RA, the ASH guideline panel suggests either eltrombopag or romiplostim

We included all systematic reviews and RCTs comparing eltrombopag and romiplostim in adults with ITP. We found no studies that directly compared eltrombopag and romiplostim in this population; thus, eltrombopag and romiplostim represent different populations. We found 1 systematic review (and update) that indirectly compared eltrombopag and romiplostim; this review reported on durable response.[5,6] A second systematic review[7] compared romiplostim vs placebo and eltrombopag vs placebo for the outcomes of major bleeding and reduction or discontinuation of corticosteroids.

Recommendation 7
In adults with ITP lasting ≥3 months who are corticosteroid-dependent or have no response to corticosteroids, the ASH guideline panel suggests either splenectomy or a TPO-RA

Recommendation 8
In adults with ITP lasting ≥3 months who are corticosteroid-dependent or have no response to corticosteroids, the ASH guideline panel suggests rituximab rather than splenectomy

Recommendation 9
In adults with ITP lasting ≥3 months who are corticosteroid-dependent or have no response to corticosteroids, the ASH guideline panel suggests a TPO-RA rather than rituximab

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