Policy Number	RX501.157
Policy Effective Date	10/01/2025

Romiplostim

Table of Contents
Coverage
Policy Guidelines
Description
Rationale
Coding
References
Policy History

Related Policies (if applicable)
RX502.061 Oncology Medications

Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of and developed by nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For HCSC members residing in the state of Ohio, § 3923.60 requires any group or individual policy (Small, Mid-Market, Large Groups, Municipalities/Counties/Schools, State Employees, Fully-Insured, PPO, HMO, POS, EPO) that covers prescription drugs to provide for the coverage of any drug approved by the U. S. Food and Drug Administration (FDA) when it is prescribed for a use recognized as safe and effective for the treatment of a given indication in one or more of the standard medical reference compendia adopted by the United States Department of Health and Human Services or in medical literature even if the FDA has not approved the drug for that indication. Medical literature support is only satisfied when safety and efficacy has been confirmed in two articles from major peer-reviewed professional medical journals that present data supporting the proposed off-label use or uses as generally safe and effective. Examples of accepted journals include, but are not limited to, Journal of

American Medical Association (JAMA), New England Journal of Medicine (NEJM), and Lancet. Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. Evidence limited to case studies or case series is not sufficient to meet the standard of this criterion. Coverage is never required where the FDA has recognized a use to be contraindicated and coverage is not required for non-formulary drugs.

Coverage

NOTE 1: This medical policy does **NOT** address oncologic indications. This medical policy **IS NOT TO BE USED** for oncologic indications. Refer to RX502.061 Oncology Medications for oncologic indications.

Hematopoietic Syndrome of Acute Radiation Syndrome (HS-ARS)
Romiplostim (Nplate®) **may be considered medically necessary:**

- To increase survival in adults and pediatric individuals (including term neonates) acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome [HS-ARS]).

Immune Thrombocytopenia
Romiplostim (Nplate®) **may be considered medically necessary** for the treatment of thrombocytopenia in (See **NOTE 2**):

- Adult individuals with immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy; or
- Pediatric individuals 1 year of age and older with ITP for at least 6 months who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.

Up to 3 mcg/kg weekly may be approved on initiations (to allow for titrations). Additional increases **may be medically necessary** if supported by evidence that the individual's platelet count is falling below 50 X 10^9/L (or 50,000/µL).

NOTE 2: Romiplostim (Nplate®) should be used only in individuals with ITP whose degree of thrombocytopenia and clinical condition increases the risk for bleeding.

Romiplostim (Nplate®) **is considered experimental, investigational and/or unproven** for all other non-Food and Drug Administration label indications, including but not limited to:

- As an attempt to normalize platelet counts.

Policy Guidelines

None.

Description

Immune Thrombocytopenia

Immune thrombocytopenia (ITP) is an autoimmune disorder distinguished by abnormally low levels of blood cells (platelets). Platelets are specialized blood cells that help maintain the integrity of the walls of blood vessels and help prevent and stop bleeding by accelerating clotting when needed. A normal platelet count ranges from about 150,000 to 400,000 per microliter (µL) of blood depending on the laboratory. Substantial bleeding does not usually occur until the platelet count is less than 50,000 or even 30,000 µL. (2)

There is no definitive laboratory test to diagnose ITP. Individuals with a platelet count lower than 100,000 µL of blood with no other reason for having low platelets, may have ITP. Measurement of anti-platelet antibody levels is not considered to be diagnostic. ITP is a diagnosis of exclusion, meaning that other causes have been considered and are either eliminated or unlikely. ITP can often be found incidentally in patients who are asymptomatic, meaning they do not have symptoms of ITP other than a low platelet count. These incidental cases may be found when a blood count is obtained during a routine yearly checkup or before a surgical procedure or during pregnancy. (2)

Often patients develop symptoms unexpectedly, such as abnormal bleeding into the skin resulting in either bruising (purpura) or tiny red dots on the skin called petechiae. Bleeding from mucous membranes such as the nose and mouth, and less commonly the stomach, gastrointestinal and urinary tracts may also occur and may subsequently result in low levels of circulating red blood cells (anemia) especially in women who are having very heavy periods (menses). (2)

ITP occurs in people of all races and ethnicities; it can occur at any age, with about 40% of all patients diagnosed with ITP being children under 10 years of age. The incidence is highest between 2 and 4 years of age, with males and females equally affected until adolescence. Between adolescence and the age of 60, ITP is more common in females. (2)

There is no well-established treatment that will cure patients with ITP; and fortunately, most patients have improved platelet counts following treatment. Initially therapy usually begins with corticosteroids (e.g., high doses of prednisone, dexamethasone, methylprednisolone) for the shortest duration possible, ideally less than 6 weeks. These drugs function by initially suppressing the clearance of antibody-coated platelets and perhaps with more prolonged use by increasing platelet production. They may also decrease the risk of bleeding by improving the function of the cells lining the blood vessels. If platelet counts do not improve after corticosteroid treatment, or when individuals present with severe bleeding, initial treatment includes adding intravenous immunoglobulin (IVIG). IVIG is typically given as needed every 2-4 weeks based on the platelet count and signs of bleeding. (2)

A second-line option is the thrombopoietin receptor agonists (TOP-Ras) that function by stimulating the body's production of platelets by megakaryocytes in the bone marrow, which release proplatelets that mature into platelets. By increasing the rate at which platelets are produced in the body, TPO-RAs may overcome the heightened rate of platelet destruction

caused by antiplatelet antibodies and their ability to impair megakaryocyte platelet production. (2)

Another second-line option is splenectomy because the spleen plays a major role in destroying antibody-covered platelets and contributes to making antiplatelet antibodies. Splenectomy initially improves platelet counts in approximately 80% of patients and can induce a long-term remission in 60%. The high long-term success rate must be weighed against the small but real increased risk of thrombosis and serious infection, which necessitates the need for appropriate vaccinations and urgent evaluation for serious febrile illnesses. (2)

Hematopoietic Syndrome of Acute Radiation Syndrome (HS-ARS)

Acute radiation syndrome (ARS), sometimes known as radiation toxicity or radiation sickness, is an acute illness caused by irradiation of the entire (or most) of the body by a high dose or penetrating radiation in a very short period of time, usually in a matter of minutes. The major cause of this syndrome is depletion of immature parenchymal stem cells in specific tissues. Examples of people who suffered from ARS are the survivors of the Hiroshima and Nagasaki atomic bombs, the firefighters that first responded after the Chernobyl Nuclear Power Plant even in 1986 and some unintentional exposures to sterilization irradiators. (3, 4)

ARS occurs hours, days, or weeks after whole-body exposure (or large partial-body exposure) to sufficient penetrating radiation to cause clinically apparent injury. Initial clinical features are non-specific and vary according to the degree and type of radiation exposure. The threshold whole-body dose for ARS in adults is approximately 1 Gray (Gy) (100 rad); lower doses are not expected to cause clinically apparent ARS. A whole-body dose of 4.5 Gy is lethal to 50 percent of exposed persons (LD50) and a dose of ≥10 Gy is typically associated with 100 percent mortality. (4)

ARS progresses through four phases, and the onset, duration of the phases, and dominant manifestations of the syndrome depend on the dose of radiation.

- Prodromal phase (0 to 2 days after exposure) refers to early generally non-specific symptoms or signs. At doses between 1 and 2 Gy, a prodrome that may include anorexia, nausea, vomiting, fatigue, tachycardia, fever and/or headache becomes evident. Early onset (e.g., <2 hours after exposure) and persistence of nausea, vomiting and/or diarrhea indicates a severe radiation exposure.
- Latent phase (2 to 20 days after exposure) is a period of improvement in prodromal symptoms. The duration of this phase is inversely related to the dose of radiation received, and patients with severe, lethal exposure may progress directly from prodromal phase to manifest illness.
- Manifest ARS (21 to 60 days after exposure) follows a predictable pattern that generally begins with infection, anemia, and bleeding, followed by uncontrollable diarrhea, hypovolemia, and electrolyte disturbances; and finally deteriorating mental status, cerebral edema, and overwhelming cardiovascular collapse.

- Recovery phase refers to the period after manifest ARS where the patient recovers from the acute exposure. Timing for recovery will depend on the severity of the injury and affected organ system(s). (4)

Even after recovery, the patient remains at risk for chronic injury and long-term complications, such as myelodysplastic syndrome, various leukemias, solid tumors (e.g., cancer of the thyroid, breast, and brain) and thyroid disease. (4)

There are four prominent subsyndromes of ARS, which may occur individually or in combination – cutaneous, hematopoietic, gastrointestinal, and neurovascular. This policy only addresses hematopoietic ARS.

For individuals who are exposed to <7 Gy radiation, hematopoietic ARS can generally be managed with supportive care, including transfusions, growth factors (cytokines), and management of infections. (5) Myeloid cytokines, such as granulocyte colony-stimulating factor (G-CSF) or granulocyte-macrophage colony-stimulating factor (GM-CSF) may be given to patients with suspected or confirmed radiation exposure ≥2 Gy. Romiplostim may be added to the myeloid cytokines to enhance hematopoietic stem cell and progenitor cell recovery. While Romiplostim has not been evaluated in humans with radiation injury (due to ethical and feasibility reasons) (1), it is beneficial in treatment of aplastic anemia and refractory immune thrombocytopenia. (5)

Regulatory Status

Romiplostim (Nplate®) is a thrombopoietin receptor agonist (TPO-RA). It increases platelet production through binding and activation of the TPO receptor, a mechanism analogous to endogenous TPO. The U.S. Food and Drug Administration (FDA) approved romiplostim (Nplate®) in 2008; it 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; and 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]). It is not indicated for the treatment of thrombocytopenia due to myelodysplastic syndrome (MDS) or any cause of thrombocytopenia other than immune thrombocytopenia; or as an attempt to normalize platelet counts. (1)

This medical policy does NOT address oncologic indications. This medical policy **IS NOT TO BE USED** for oncologic indications. Refer to RX502.061 Oncology Medications for oncologic indications.

Rationale

This policy is based on the U.S. Food and Drug Administration (FDA) labeled indications for Nplate® (romiplostim).

Adults with Immune Thrombocytopenia (ITP) (1)
The safety and efficacy of Nplate in adults with ITP were assessed in two double-blind, placebo-controlled clinical studies, an open-label single-arm study, and in an open-label extension study.

Studies 1 (NCT00102336) and 2 (NCT00102323)
In Studies 1 and 2, patients with ITP who had completed at least one prior treatment and had a platelet count of ≤ 30×10^9/L prior to study entry were randomized (2:1) to 24 weeks of Nplate (1 mcg/kg subcutaneous [SC]) or placebo. The median time since ITP diagnosis for Studies 1 and 2 was 2.1 years (range 0.1 to 31.6) and 8 years (range 0.6 to 44.8), respectively. Prior ITP treatments in both study groups included corticosteroids, immunoglobulins, rituximab, cytotoxic therapies, danazol, and azathioprine. Patients already receiving ITP medical therapies at a constant dosing schedule were allowed to continue receiving these medical treatments throughout the studies. Rescue therapies (i.e., corticosteroids, intravenous immunoglobulins [IVIG], platelet transfusions, and anti-D immunoglobulin) were permitted for bleeding, wet purpura, or if the patient was at immediate risk for hemorrhage. Patients received single weekly SC injections of Nplate, with individual dose adjustments to maintain platelet counts (50×10^9/L to 200×10^9/L).

Study 1 evaluated patients who had not undergone a splenectomy. The patients had been diagnosed with ITP for approximately 2 years and had received a median of three prior ITP treatments. Overall, the median platelet count was 19×10^9/L at study entry. During the study, the median weekly Nplate dose was 2 mcg/kg (25th–75th percentile: 1–3 mcg/kg).

Study 2 evaluated patients who had undergone a splenectomy. The patients had been diagnosed with ITP for approximately 8 years and had received a median of six prior ITP treatments. Overall, the median platelet count was 14×10^9/L at study entry. During the study, the median weekly Nplate dose was 3 mcg/kg (25th–75th percentile: 2–7 mcg/kg).

Study 1 and 2 outcomes are shown in Table 1. A durable platelet response was the achievement of a weekly platelet count ≥ 50×10^9/L for any 6 of the last 8 weeks of the 24-week treatment period in the absence of rescue medication at any time. A transient platelet response was the achievement of any weekly platelet counts ≥ 50×10^9/L for any 4 weeks during the treatment period without a durable platelet response. An overall platelet response was the achievement of either a durable or a transient platelet response. Platelet responses were excluded for 8 weeks after receiving rescue medications.

Table 1. Results from Placebo-Controlled Studies[a]

Outcomes	Study 1 Non-splenectomized Patients	Study 2 Splenectomized Patients

	Nplate (n=41)	Placebo (n=21)	Nplate (n=42)	Placebo (n=21)
Platelet Responses and Rescue Therapy				
Durable Platelet Response, n (%)	25 (61%)	1 (5%)	16 (38%)	0 (0%)
Overall Platelet Response, n (%)	36 (88%)	3 (14%)	33 (79%)	0 (0%)
Number of Weeks with Platelet Counts ≥ 50 × 10^9/L, average	15	1	12	0
Requiring Rescue Therapy, n (%)	8 (20%)	13 (62%)	11 (26%)	12 (57%)
Reduction/Discontinuation of Baseline Concurrent ITP Medical Therapy				
Receiving Therapy at Baseline	(n=11)	(n=10)	(n=12)	(n=6)
Patients Who Had > 25% Dose Reduction in Concurrent Therapy, n (%)	4/11 (36%)	2/10 (20%)	4/12 (33%)	1/6 (17%)
Patients Who Discontinued Baseline Therapy, n (%)[b]	4/11 (36%)	3/10 (30%)	8/12 (67%)	0/6 (0%)

ITP: immune thrombocytopenia.
[a] All *p* values <0.05 for platelet response and rescue therapy comparisons between Nplate and placebo.
[b] For multiple concomitant baseline therapies, all therapies were discontinued.

In Studies 1 and 2, nine patients reported a serious bleeding event [five (6%) Nplate, four (10%) placebo]. Bleeding events that were Grade 2 severity or higher occurred in 15% of patients treated with Nplate and 34% of patients treated with placebo.

Study 3 (NCT01143038)

Study 3 was a single-arm, open-label study designed to assess the safety and efficacy of Nplate in adult patients who had an insufficient response (platelet count ≤ 30 x 10^9/L) to first-line therapy. The study enrolled 75 patients of whom the median age was 39 years (range 19 to 85) and 59% were female.

The median time from ITP diagnosis to study enrollment was 2.2 months (range 0.1 to 6.6). Sixty percent of patients had ITP duration < 3 months and 40% had ITP duration ≥ 3 months. The median platelet count at screening was 20 x 10^9/L. Prior ITP treatments included corticosteroids, immunoglobulins, and anti-D immunoglobulins. Patients already receiving ITP medical therapies at a constant dosing schedule were allowed to continue receiving these medical treatments throughout the studies. Rescue therapies (i.e., corticosteroids, IVIG, platelet transfusions, anti-D immunoglobulin, dapsone, danazol, and azathioprine) were permitted.

Patients received single weekly SC injections of Nplate over a 12-month treatment period, with individual dose adjustments to maintain platelet counts (50 x 10^9/L to 200 x 10^9/L). During the study, the median weekly Nplate dose was 3 mcg/kg (25th-75th percentile: 2-4 mcg/kg).

Of the 75 patients enrolled in Study 3, 70 (93%) had a platelet response ≥ 50 x 10^9/L during the 12-month treatment period. The mean number of months with platelet response during the 12-

month treatment period was 9.2 (95% CI: 8.3, 10.1) months; the median was 11 (95% CI: 10, 11) months. The Kaplan-Meier estimate of the median time to first platelet response was 2.1 weeks (95% CI: 1.1, 3.0). Twenty-four (32%) patients maintained every platelet count ≥ 50 x 10^9/L for at least 6 months in the absence of Nplate and any medication for ITP (concomitant or rescue); the median time to onset of maintaining every platelet count ≥ 50 x 10^9/L for at least 6 months was 27 weeks (range 6 to 57).

Study 4 (NCT00116688) Extension Study

Patients who had completed a prior Nplate study (including Study 1 and Study 2) were allowed to enroll in a long-term open-label extension study. Following Nplate discontinuation in Studies 1 and 2, seven patients maintained platelet counts of ≥ 50 × 10^9/L. Among 291 patients who subsequently entered the extension study and received Nplate, platelet counts were increased and sustained regardless of whether they had received Nplate or placebo in the prior placebo-controlled studies. The majority of patients reached a median platelet count of 50 × 10^9/L after receiving one to three doses of Nplate, and these platelet counts were maintained throughout the remainder of the study with a median duration of Nplate treatment of 78 weeks and a maximum duration of 277 weeks.

Pediatric Patients with Immune Thrombocytopenia (ITP) (1)

The safety and efficacy of Nplate in pediatric patients 1 year and older with ITP for at least 6 months were assessed in two double-blind, placebo-controlled clinical trials.

Study 5 (NCT01444417)

In Study 5, patients refractory or relapsed after at least one prior ITP therapy with a platelet count ≤ 30 x 10^9/L were stratified by age and randomized (2:1) to receive Nplate (n = 42) or placebo (n = 20). The starting dose for all ages was 1 mcg/kg weekly. Over a 24-week treatment period, dose was titrated up to a maximum of 10 mcg/kg weekly of either Nplate or placebo in an effort to maintain a target platelet count of ≥ 50 × 10^9/L to 200 × 10^9/L.

The median age of the patients was 9.5 years (range 3 to 17) and 57% were female. Approximately 58% of patients had a baseline count ≤ 20 x 10^9/L, which was similar between treatment arms. The percentage of patients with at least 2 prior ITP therapies (predominantly immunoglobulins and corticosteroids) was 81% in the group treated with Nplate and 70% in the group treated with placebo. One patient in each group had undergone splenectomy.

Study 5 results are shown in Table 2. The efficacy of Nplate in this trial was measured by the proportion of patients receiving Nplate achieving a durable platelet response and the proportion of patient achieving an overall platelet response. A durable platelet response was defined as achieving at least 6 weekly platelet counts ≥ 50 × 10^9/L during weeks 18 through 25 of treatment. A transient platelet response was defined as a weekly platelet count ≥ 50 × 10^9/L for 4 or more times during weeks 2 through 25, but without durable platelet response. An overall platelet response was defined as a durable or a transient platelet response. Platelet responses were excluded for 4 weeks after receiving rescue medications.

Table 2. Results from Pediatric Placebo-Controlled Studies[a]

Outcomes	Study 5	
	Nplate (n=42)	**Placebo (n=20)**
Platelet Responses and Rescue Therapy		
Durable Platelet Response[a], n (%)	22 (52%)	2 (10%)
Overall Platelet Response[a], n (%)	30 (71%)	4 (20%)
Number of Weeks with Platelet Counts ≥ 50 x 10^9/L, median[a]	12	1

[a] All *p* values <0.05 for platelet response between Nplate and placebo.

Study 6 (NCT00515203)

In study 6, patients diagnosed with ITP at least 6 months prior to enrollment with a platelet count ≤ 30 x 10^9/L were stratified by age and randomized (3:1) to receive Nplate (n = 17) or placebo (n = 5). The starting dose for all ages was 1 mcg/kg weekly. Over a 12-week treatment period dose was titrated up to a maximum of 10 mcg/kg weekly of either Nplate or placebo in an effort to maintain a target platelet count of ≥ 50 × 10^9/L to 250 × 10^9/L.

The median age of the patients was 10 years (range 1 to 17 years) and 27.3% of patients were female. Approximately 82% of patients had a baseline count ≤ 20 x 10^9/L, which was similar between treatment arms. The percentage of patients with at least 2 prior ITP therapies (predominantly IVIG and corticosteroids) was 88% in the group treated with Nplate and 100% in the group treated with placebo. Six patients in the Nplate group and 2 patients in the placebo group had undergone splenectomy.

The efficacy of Nplate in this trial was measured by the proportion of patients who achieved a platelet count of ≥ 50 × 10^9/L for 2 consecutive weeks and by the proportion of patients who achieved an increase in platelet count of ≥ 20 × 10^9/L above baseline for 2 consecutive weeks. Platelet responses within 4 weeks following rescue medications use were excluded. Of the 17 patients who received romiplostim, 15 achieved a platelet count of ≥ 50 × 10^9/L for 2 consecutive weeks (88.2%, 95% CI: 63.6%, 98.5%).

The same 15 patients also achieved an increase in platelet count of ≥ 20 × 10^9/L above baseline for 2 consecutive weeks during the treatment period (88.2%, 95% CI: 63.6%, 98.5%). None of the patients treated with placebo achieved either endpoint.

Study 7 (NCT02279173) Long-Term Pediatric Study

In study 7, patients diagnosed with ITP at least 6 months prior to enrollment and who received at least 1 prior ITP therapy or were ineligible for other ITP therapies were enrolled to a study to evaluate efficacy for up to 3 years. Nplate was administered weekly for up to 3 years by subcutaneous injection starting at a dose of 1 mcg/kg with weekly increments to a maximum dose of 10 mcg/kg to reach a target platelet count between 50 x 10^9/L and 200 x 10^9/L. The median age of the patients was 10 years (range 1 to 17 years), and the median and maximum duration of treatment were 156 weeks and 163 weeks, respectively. Among the 203 patients,

the mean (SD) and median percentage of time with a platelet response (platelet count ≥ 50 x 10^9/L) within the first 6 months of initiation of Nplate without rescue medication use for the past 4 weeks was 50.6% (37) and 50.0%, respectively. Sixty (29.6%) subjects overall received rescue medications. Rescue medications (i.e., corticosteroids, platelet transfusions, IVIG, azathioprine, anti-D immunoglobulin, and danazol) were permitted.

Hematopoietic Syndrome of Acute Radiation Syndrome (HS-ARS) (1)
Efficacy studies of Nplate could not be conducted in humans with acute radiation syndrome for ethical and feasibility reasons. Approval for this indication was based on efficacy studies conducted in animals, Nplate's effect on platelet count in healthy human volunteers and on data supporting Nplate's effect on thrombocytopenia in patients with ITP and insufficient response to corticosteroids, immunoglobulins, or splenectomy.

Because of the uncertainty associated with extrapolating animal efficacy data to humans, the selection of a human dose for Nplate is aimed at providing platelet response to Nplate that is similar to that observed in efficacy studies conducted in animals. The recommended dose of Nplate for patients exposed to myelosuppressive doses of radiation is 10 mcg/kg administered once as a subcutaneous injection. The 10 mcg/kg dosing regimen for humans is based on population modeling and simulation analyses. For pediatric patients (including term neonates), extrapolation was based on data supporting Nplate's effect on thrombocytopenia in patients with ITP and an insufficient response to corticosteroids, immunoglobulins, or splenectomy.

The safety of Nplate for the acute radiation syndrome setting was assessed based on the clinical experience in patients with ITP and from a study with healthy volunteers. The efficacy of Nplate was studied in a randomized, blinded, placebo-controlled study in a non-human primate model of radiation injury. Rhesus monkeys were randomized to either a control (n = 40) or treated (n = 40) cohort. Animals were exposed to total body irradiation (TBI) of 6.8 Gy from a $Cobalt^{60}$ gamma ray source, representing a dose that would be lethal in 70% of animals by 60 days of follow-up ($LD_{70/60}$). Animals were administered a single subcutaneous dose of blinded treatment (control article [sterile saline] or Nplate [5mg/kg]) 24 hours post-irradiation. The primary efficacy endpoint was survival. Animals received medical management consisting of intravenous or subcutaneous fluids, anti-ulcer medication, anti-emetic medication, analgesics, antimicrobials, and other support as required.

Nplate significantly (one-sided p = 0.0002) increased 60-day survival in the irradiated animals: 72.5% survival (29/40) in the Nplate group compared to 32.5% survival (13/40) in the control group. In the same study, an exploratory cohort of n=40 animals received Nplate (5mg/kg) on day 1 and pegfilgrastim (0.3mg/kg) on days 1 and 8 post-irradiation. Survival in this combined treatment group was 87.5% (95% CI: 73.2%, 95.8%).

Summary of Evidence
Based on a review of the clinical trials provided to the U.S. Food and Drug Administration (FDA) for approval, romiplostim (Nplate®) may be considered medically necessary 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; and 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 (Nplate®) is considered experimental, investigational and/or unproven for all other non-U.S. FDA labeled indications, including but not limited to an attempt to normalize platelet counts.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	J2802 [Deleted 1/2025: J2796]

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

References

U.S. Food and Drug Administration Label:

1. FDA – Nplate® (romiplostim) Highlights of Prescribing Information. U.S. Food and Drug Administration: Prescribing Information (February 2025). Available at <https://www.accessdata.fda.gov> (accessed June 9, 2025).

Other:

2. NORD. Immune Thrombocytopenia. National Organization for Rare Diseases. July 2022. Available at <https://www.rarediseases.org> (accessed July 16, 2025).
3. CDC – Acute Radiation Syndrome: Information for clinicians. Centers for Disease Control and Prevention. April 23, 2024. Available at <https://www.cdc.gov> (accessed July 16, 2025).
4. Dainiak N, Wingard JR, Kazzi Z. Clinical manifestations, evaluation, and diagnosis of acute radiation exposure. In: UpToDate, Danzl DF, Chao NJ (Eds), UpToDate, Waltham, MA. Available at <https://www.uptodate.com> (accessed July 16, 2025).
5. Wingard JR, Dainiak N, Kazzi Z. Management of radiation injury. In: UpToDate, Danzl DF, Chao NJ (Eds), UpToDate, Waltham, MA. Available at <https://www.uptodate.com> (accessed July 16, 2025).

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision	
Date	**Description of Change**
10/01/2025	Document updated with literature review. The following changes were made to Coverage: 1) Editorial change to "Immune Thrombocytopenia" medically necessary statement bullets; 2) Added the phrase "non-Food and Drug Administration Label" to the experimental investigational and/or unproven statement. No new references added, some updated.
10/01/2024	Document updated with literature review. The following change was made to Coverage: Added "Up to 3 mcg/kg weekly may be approved on initiations (to allow for titrations). Additional increases may be medically necessary if supported by evidence that the individual's platelet count is falling below 50 X 10^9/L (or 50,000/µL)." to the criteria for Immune Thrombocytopenia. References updated; none added.
04/01/2024	New medical document. NOTE 1: This medical policy does NOT address oncologic indications. This medical policy IS NOT TO BE USED for oncologic indications. Refer to RX502.061 Oncology Medications for oncologic indications. Hematopoietic Syndrome of Acute Radiation Syndrome (HS-ARS) Romiplostim (Nplate®) may be considered medically necessary: 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]). Immune Thrombocytopenia (ITP) Romiplostim (Nplate®) may be considered medically necessary for the treatment of thrombocytopenia in (See NOTE 2): 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 immune thrombocytopenia (ITP) for at least 6 months who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. NOTE 2: Romiplostim (Nplate®) should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increases the risk for bleeding. Romiplostim (Nplate®) is considered experimental, investigational and/or unproven for all other indications, including but not limited to: As an attempt to normalize platelet counts.