Medical Benefit Drug Policy

Nplate® (romiplostim) Injection

Policy Number: MC/PC 027
Effective Date: March 1, 2025

Instructions for Use

Table of Contents **Page**

Coverage Rationale 1
Applicable Codes 2
Background 2
Clinical Evidence 2
U.S. Food and Drug Administration 4
References 4
Policy History/Revision Information 5
Instructions for Use 5

Related Policies

- n/a

Coverage Rationale

Immune Thrombocytopenia (ITP)

For initial coverage of Nplate (romiplostim) for Immune Thrombocytopenia (ITP), the following will be required:

- Diagnosis of one of the following:
  - Immune thrombocytopenia (ITP)
  - Relapsed/refractory ITP **and**
- Baseline platelet count is less than 30,000/mcL **and**
- Patient's degree of thrombocytopenia and clinical condition increase the risk of bleeding **and**
- Trial and failure, contraindication, or intolerance to one of the following:
  - Corticosteroids (e.g., dexamethasone, prednisone)
  - Immune globulins (e.g. Gammaplex, Gammagard S/D)
  - Splenectomy **and**
- Prescribed by or in consultation with a hematologist/oncologist

For reauthorization coverage of Nplate (romiplostim), the following will be required:

- Patient demonstrates positive response to therapy as evidenced by an increase in platelet count to a level sufficient to avoid clinically important bleeding

Hematopoietic Syndrome of Acute Radiation Syndrome

For initial coverage of Nplate (romiplostim) for Hematopoietic Syndrome of Acute Radiation Syndrome, the following will be required:

- Diagnosis of hematopoietic syndrome of acute radiation syndrome **and**
- Patient is acutely exposed to myelosuppressive doses of radiation **and**
- Prescribed by or in consultation with a hematologist/oncologist

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J2796	Injection, Romiplostim, 10 micrograms

ICD-10 Code	Description
D69.3	Immune thrombocytopenic purpura

Background

Primary immune thrombocytopenia (ITP), also called idiopathic thrombocytopenic purpura or immune thrombocytopenic purpura, is an acquired thrombocytopenia caused by autoantibodies against platelet antigens (Arnold & Cuker 2024). The prevalence of ITP is approximately 12 per 100,000. ITP diagnosis is classified as primary or as secondary (to another disease) and as acute (of six months or less in duration) or chronic (12 months or greater). Adult and childhood ITP present with different symptoms. Healthy children often present with onset of petechiae or purpura after an illness. In most children (70%), the illness will have resolved by 6 months with or without treatment. ITP in adults is usually chronic and the onset is often insidious (Arnold et al 2024)

The pathogenesis of ITP is related to a combination of impaired platelet production and increased platelet destruction caused primarily by antiplatelet autoantibodies. An immune basis for ITP matches characteristics of the disease treatment including the efficacy of intravenous immune globulin and shortened survival of transfused platelets due to their rapid destruction. A second finding forced a change in the understanding of ITP: Thrombopoietin receptor agonists (TPO-RA). TPO-RA works by stimulating the TPO receptor causing an increase in the production of megakaryocytes and platelets. The efficacy of TPO-RA matches other labelled autologous platelet studies that showed insufficient platelet production as likely another mechanism of thrombocytopenia in ITP.

Clinical Evidence

Immune Thrombocytopenia (ITP)

A systematic review and meta-analysis of 13 RCTs (N = 1126) evaluated the safety and efficacy of eltrombopag and romiplostim in patients with primary ITP (Wang et al 2016). All of the included studies enrolled patients with persistent or chronic ITP with platelet counts ≤ 30 x 109/L (with the exception of 1 study enrolling patients with platelet counts < 50 x 109/L). Four studies evaluated eltrombopag in adults and 2 were conducted in children. The durations of romiplostim and eltrombopag treatment ranged from 6 to 52 weeks and 6 to 26 weeks, respectively.

- The pooled results indicated that romiplostim and eltrombopag significantly increased platelet response and durable response vs control: risk ratio (RR), 2.77; 95% CI, 2.01 to 3.82; p = 5.9 x 10−10 and RR, 7.52; 95% CI, 3.94 to 14.35; p = 9.2 x 10−10, respectively, and that romiplostim and eltrombopag significantly reduced the incidence of any or severe bleeding events: RR, 0.80; 95% CI, 0.67 to 0.95; p = 0.013 and RR, 0.52; 95% CI, 0.27 to 0.99; p = 0.048, respectively.
- Subgroup meta-analysis demonstrated that both romiplostim and eltrombopag were associated with higher rates of response, with RR, 2.43; 95% CI, 1.40 to 4.22; and RR, 3.01; 95% CI, 2.28 to 3.99, respectively, durable response (RR, 8.83; 95% CI, 2.19 to 35.61; and RR, 7.21; 95% CI, 3.25 to 15.96, respectively), and that

romiplostim and eltrombopag substantially increased the rates of response or durable response in children (RR, 2.49; 95% CI, 1.46 to 4.23; and RR, 7.64; 95% CI, 2.73 to 21.36, respectively).

- The rate of response was similar between splenectomized and non-splenectomized patients receiving romiplostim and eltrombopag (RR, 0.84; 95% CI, 0.49 to 1.42); however, the rate of durable response was significantly lower in splenectomized patients than in non-splenectomized patients (RR, 0.72; 95% CI, 0.54 to 0.95; p = 0.022).
- Romiplostim and eltrombopag were also associated with a significant reduction in the proportion of patients requiring rescue medications (RR, 0.50; 95% CI, 0.42 to 0.59; p = 2.0 x 10-15).
- Based on the pooled results of 3 studies, there was a significant increase in the proportion of patients who were able to reduce or discontinue their concurrent ITP therapies in the Thrombopoietin Receptor Agonists (TPO-RA) group compared with the control group (RR, 1.85; 95% CI, 1.13 to 3.01; p = 0.014).
- The rates of any or serious AEs (SAEs) were similar between the TPO-RA and control groups (RR, 1.01; 95% CI, 0.92 to 1.10; and RR, 0.74; 95% CI, 0.54 to 1.01, respectively).

Acute Radiation Syndrome

Efficacy studies of romiplostim 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, 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 (Nplate prescribing information 2022).

Clinical Guidelines:

Clinical guidelines that provide recommendations for the treatment of ITP in adults and children include the American Society of Hematology (ASH) 2019 evidence-based practice guideline for ITP (Neunert et al 2019) and the international consensus report on the investigation and management of primary ITP (Provan et al 2019).

- The goal of all treatment strategies for ITP in children, or in adults, is to achieve a platelet count that is associated with adequate hemostasis, rather than a "normal" platelet count.
- The decision to initiate treatment in adults with ITP should be based on the individual patient's severity of bleeding and bleeding risk. ASH suggests that treatment be administered for newly diagnosed patients with a platelet count < 30 x 109/L. The international consensus guidelines state that treatment is rarely indicated in patients with platelet counts > 20 x 109/L in the absence of bleeding due to platelet dysfunction or other factors such as another known or unknown hemostatic defect, trauma, or surgery.
- Initial first-line pharmacologic treatment options for ITP include corticosteroids and either intravenous immune globulin (IVIG) or intravenous anti-D (in appropriate patients) if corticosteroids are contraindicated. IVIG may be used with corticosteroids when a more rapid increase in platelet count is required.
- Second-line therapy options for ITP include splenectomy, TPO-RAs, and rituximab. According to ASH:
    - Either splenectomy or a TPO-RA is suggested.
    - Rituximab is suggested rather than splenectomy.
    - A TPO-RA is suggested rather than rituximab.
- Each of these second-line treatments may be effective therapy; the choice of treatment should be individualized based on duration of ITP, frequency of bleeding episodes requiring hospitalization or rescue medication, comorbidities, patient age, medication adherence, medical and social support networks, patient values and preferences, cost, and availability.
- The international consensus report was updated for 2019, with major changes in the use of rituximab, TPO-RAs, and fostamatinib for subsequent treatment of ITP in adults. The main goal of subsequent treatment is to attain a sustained increase in the platelet count that is considered hemostatic for the individual patient while minimizing AEs and allowing for the possibility of attaining a remission.
- TPO-RAs including eltrombopag, avatrombopag, and romiplostim have provided excellent responses (> 60%) in splenectomized and non-splenectomized patients. Response can persist up to 6 to 8 years and often allow other ITP therapies to be reduced or discontinued. Cessation of treatment will lead to the return of

thrombocytopenia in most cases, but some patients (10% to 30%) may achieve a durable response after TPO-RAs are tapered and withdrawn.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Nplate® is a thrombopoietin receptor agonist indicated for the treatment of thrombocytopenia in the following:

- 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.

References

1. Nplate® [prescribing information]. Thousand Oaks, CA: Amgen; February 2022.
2. American Society of Hematology 2019 guidelines for immune thrombocytopenia. Available at: https://ashpublications.org/bloodadvances/article/3/23/3829/429213/American-Society-of-Hematology-2019-guidelines-for. Accessed January 21, 2025.
3. Cines DB, Blanchette VS. Immune thrombocytopenic purpura. New England Journal of Medicine 2002; 346:995-1008.
4. Arnold DM, Cuker A. Immune thrombocytopenia (ITP) in adults: Clinical manifestations and diagnosis. UpToDate Web site. 2025. Last updated July 10, 2024. http://www.uptodate.com. Accessed January 21, 2025.
5. InterQual 2020, April 2020 Release CP: Specialty Rx Non-Oncology, 2021 Change Healthcare LLC.
6. Kuter DJ, Bussel JB, Lyons RM, et al. Efficacy of romiplostim in patients with chronic immume thrombocytopenic purpura: a double-blind randomised controlled trial. Lancet. 2008; 371:395-403.
7. Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Adv. 2019;3(23):3829-3866.
8. Provan D, Arnold DM, Bussel JB, et al. Updated international consensus report on the investigation and management of primary immune thrombocytopenia. Blood Adv. 2019; 3(22): 3780-3817.
9. Toltl LJ, Arnold DM. Pathophysiology and management of chronic immune thrombocytopenia. British Journal of Hematology 2011; 152:52-60.
10. Wang L, Gao Z, Chen XP, Zhang HY, et al. Efficacy and safety of thrombopoietin receptor agonists in patients with primary immune thrombocytopenia: A systematic review and meta-analysis. *Sci Rep.* 2016;6:39003. doi: 10.1038/srep39003.

Policy History/Revision Information

Date	Summary of Changes
12/13/2023	Approved by OptumRx P&T Committee
2/15/2024	Annual Review. No changes made. Updated references.
2/20/2025	Annual Review. No changes made. Updated references.

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. The insurance reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

OptumRx may also use tools developed by third parties to assist us in administering health benefits. OptumRx Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

Archived Policy Versions (Internal Only)

Effective Date	Policy Number	Policy Title
mm/dd/yyyy – mm/dd/yyyy	######	Title of Policy Hyperlinked to KL or Other Internal Location

Nondiscrimination & Language Access Policy

Discrimination is Against the Law. Aspirus Health Plan, Inc. complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex, (including sex characteristics, including intersex traits; pregnancy or related conditions; sexual orientation, gender identity and sex stereotypes), consistent with the scope of sex discrimination described at 45 CFR § 92.101(a)(2). Aspirus Health Plan, Inc. does not exclude people or treat them less favorably because of race, color, national origin, age, disability, or sex.

Aspirus Health Plan, Inc.:
Provides people with disabilities reasonable modifications and free appropriate auxiliary aids and services to communicate effectively with us, such as:

- Qualified sign language interpreters.
- Written information in other formats (large print, audio, accessible electronic formats, other formats).

Provides free language assistance services to people whose primary language is not English, which may include:

- Qualified interpreters.
- Information written in other languages.

If *you* need reasonable modifications, appropriate auxiliary aids and services, or language assistance services, contact the Nondiscrimination Grievance Coordinator at the address, phone number, fax number, or email address below.

If *you* believe that Aspirus Health Plan, Inc. has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, *you* can file a *grievance* with:

Nondiscrimination Grievance Coordinator
Aspirus Health Plan, Inc.
PO Box 1890
Southampton, PA 18966-9998
Phone: 1-866-631-5404 (TTY: 711)
Fax: 763-847-4010
Email: customerservice@aspirushealthplan.com

You can file a *grievance* in person or by mail, fax, or email. If *you* need help filing a *grievance*, the Nondiscrimination Grievance Coordinator is available to help *you*.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1.800.368.1019, 800.537.7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html. This notice is available at Aspirus Health Plan, Inc.'s website: https://aspirushealthplan.com/webdocs/70021-AHP-NonDiscrim_Lang-Assist-Notice.pdf.

Language Assistance Services

Albanian: KUJDES: Nëse flitni shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë.Telefononi në 1-800-332-6501 (TTY: 711).

Arabic تنبيه: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية متاحة لك مجاناً. اتصل بن اعلى رقم الهاتف1-800-332-6501(رقم هاتف الصم والبك : 711)

French: ATTENTION: Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1-800-332-6501 (ATS: 711).

German: ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zurVerfügung. Rufnummer: 1-800-332-6501 (TTY: 711).

Hindi: _यान द_: य_द आप ि हंदी बोलते ह_ तो आपके ि लए मु_त म_ भाषा सहायता सेवाएं उपल_ध ह_।1-800-332-6501 (TTY: 711) पर कॉल कर_।

Hmong: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1-800-332-6501 (TTY: 711).

Korean: 주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다.1-800-332-6501 (TTY: 711)번으로 전화해 주십시오.

Polish: UWAGA: Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer1-800-332-6501 (TTY: 711).

Russian: ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода.Звоните 1-800-332-6501 (телетайп: 711).

Spanish: ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al1-800-332-6501 (TTY: 711).

Tagalog: PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nangwalang bayad. Tumawag sa 1-800-332-6501 (TTY: 711).

Traditional Chinese: 注意：如果您使用繁體中文， 您可以免費獲得語言援助服務。請 致電 1-800-332-6501 (TTY: 711)

Vietnamese: CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-800-332-6501 (TTY: 711).

Pennsylvania Dutch: Wann du Deitsch (Pennsylvania German / Dutch) schwetzscht, kannscht du mitaus Koschte ebbergricke, ass dihr helft mit die englisch Schprooch. Ruf selli Nummer uff: Call 1-800-332-6501 (TTY: 711).

Lao: ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ,ໂດຍບໍ່ເສັງຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1-800-332-6501 (TTY: 711).

70021 07-24 ©2024 Aspirus Health Plan, Inc. All rights reserved.