Clinical Policy: romiplostim (Nplate), eltrombopag (Promacta)

Reference Number: CP.CPA.104
Effective Date: 11.16.16
Last Review Date: 11.17 Revision Log
Line of Business: Medicaid – Medi-Cal

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The following are thrombopoietin receptor agonists requiring prior authorization: romiplostim (Nplate™), eltrombopag (Promacta®).

FDA approved indication
Nplate and Promacta are indicated for the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenic purpura (ITP) who have had an insufficient response to corticosteroids, immunoglobulins or splenectomy.

Limitation of use:
Nplate and Promacta
- Should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding.
- Should not be used in an attempt to normalize platelet counts.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Nplate or Promacta is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Idiopathic Thrombocytopenic Purpura (ITP) (must meet all)**:**
1. Diagnosis of ITP (chronic, relapsed, or refractory) with an increased risk for bleeding based on the degree of thrombocytopenia and clinical condition;
2. Request is for Promacta or Nplate;
3. Dose does not exceed: 10 mcg/kg/week (Nplate); 75 mg/day (Promacta).

Approval duration:
Promacta: Length of benefit
Nplate: 6 months or to member's renewal period, whichever is longer.

B. Chronic Hepatitis C Thrombocytopenia (must meet all)**:**
1. Diagnosis of thrombocytopenia in patients with chronic hepatitis C;
2. Request is for Promacta;

3. Therapy is required to allow initiation or maintenance of interferon-based therapy with ribavirin;
4. Dose does not exceed: 100 mg/day.

Approval duration: Length of benefit to coincide with duration of peg-interferon/ribavirin.

C. Severe Aplastic Anemia (must meet all)**:**
1. Diagnosis of severe aplastic anemia with an insufficient response to immunosuppressive therapy;
2. Request is for Promacta;
3. Dose does not exceed: 150 mg/day.

Approval duration: Length of benefit

D. Other diagnoses/indications:
1. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Documentation of positive response to therapy (e.g., patient maintains target platelet count);
3. If request is for a dose increase, new dose does not exceed:
   a. ITP: 10 mcg/kg/week (Nplate); 75 mg/day (Promacta);
   b. HepC (Promacta): 100 mg/day;
   c. Aplastic anemia (Promacta): 150 mg/day.

Approval duration: Length of benefit

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy;
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.PHAR.57 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
ALT: alanine aminotransferase
AST: aspartate aminotransferase
ITP: thrombocytopenic purpura

TPO: thrombopoietin
ULN: upper limit of normal

Appendix B: General Information

- Promacta should not be used to normalize platelet counts. In patients with chronic hepatitis C, Promacta should be used only in patients whose degree of thrombocytopenia prevents the initiation of interferon therapy or limits the ability to maintain optimal interferon-based therapy.
- Black Box Warning (Promacta): risk for hepatotoxicity.
  - Measure serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin prior to initiation, every two weeks during the dose adjustment phase and monthly following establishment of a stable dose. If bilirubin is elevated, perform fractionation.
  - Evaluate abnormal serum liver tests with repeat testing within 3 to 5 days. If abnormalities are confirmed, monitor serm liver tests weekly until the abnormalities resolve, stabilize, or return to baseline levels.
  - Discontinue Promacta if ALT levels increase to ≥3x upper limit of normal (ULN) and are one of the following:
    - Progressive;
    - Persistent for ≥4 weeks;
    - Accompanied by increased direct bilirubin;
    - Accompanied by clinical symptoms of liver injury or evidence for hepatic decompensation

Appendix C: Therapeutic Alternatives

Drug	Dosing Regimen	Maximum Dose
cyclosporine	Dosage varies for treatment of aplastic anemia.	Varies
methylprednisolone	Dosage varies for treatment of aplastic anemia.	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Eltrombopag (Promacta)	ITP	50 mg PO QD for most adult and pediatric patients 6 years and older; reduce initial dose in patients of East Asian ancestry or patients with hepatic insufficiency. 25 mg PO QD for pediatric patients aged 1 to 5 years; reduce initial dose	75 mg/day

<table>
<tr><td></td><td></td><td colspan="2">in patients of East Asian ancestry or patients with hepatic insufficiency.</td><td></td></tr>
<tr><td>Eltrombopag (Promacta)</td><td>Chronic Hepatitis C Thrombocytopenia</td><td colspan="2">25 mg PO QD
Adjust to achieve a target platelet count required to initiate antiviral therapy.

<table><tr><th>Platelet Count Result</th><th>Dose Adjustment or Response</th></tr><tr><td><50 x 10^9/L following at least 2 weeks of Promacta.</td><td>Increase daily dose by 25 mg (maximum of 100 mg/day)</td></tr><tr><td>≥200 x 10^9/L to ≤400 x 10^9/L at any time.</td><td>Decrease the daily dose by 25 mg.</td></tr><tr><td>>400 x 10^9/L</td><td>Stop Promacta; increase the frequency of platelet monitoring to twice weekly.

Once the platelet count is <150 x 10^9/L, reinitiate Promacta at a daily dose reduced by 25 mg.

For patients taking the 25 mg PO QD, reinitiate Promacta at a daily dose of 12.5 mg.</td></tr><tr><td>>400 x 10^9/L after 2 weeks of therapy at lowest dose of Promacta.</td><td>Discontinue Promacta.</td></tr></table></td><td>100 mg/day</td></tr>
<tr><td>Eltrombopag (Promacta)</td><td>Aplastic Anemia</td><td colspan="2">50 mg PO QD for most patients; reduce initial dose for patients of</td><td>150 mg/day</td></tr>
</table>

		East Asian ancestry or patients with hepatic insufficiency.	
Romiplostim (Nplate)	ITP	1 mcg SC one time per week.	10 mcg/kg/day

VI. Product Availability

Drug	Availability
Promacta	Tablet: 12.5 mg, 25 mg, 50 mg, 75 mg
Nplate	Single-Use Vials: 250 mcg, 500 mcg

VII. References

1. Promacta [Prescribing information] Research Triangle Park, NC: GlaskoSmithKline; September 2015. Accessed January 12, 2017.
2. Nplate [Prescribing information] Thousand Oaks, CA: Amgen; April 2016. Accessed January 12, 2017.
3. Bussel JB, Cheng G, Saleh MN, et al. Eltrombopag for the treatment of chronic idiopathic thrombocytopenic purpura. N Engl J Med 2007;357(22):2237-2247.
4. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed January 12, 2017.
5. Promacta. American Hospital Formulary Service Drug Information. Available at:http://www.medicinescomplete.com/mc/ahfs/current/. Accessed January 12, 2017.
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7. GlaxoSmithKline. Date on File. Study TPL103922/ENABLE 1 and TPL108390/ENABLE 2. (RMT4083). 2011.
8. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org. Accessed July 7, 2016.
9. Nplate Drug Monograph. Clinical Pharmacology. Accessed January 12, 2017. http://www.clinicalpharmacology-ip.com
10. Promacta Drug Monograph. Clinical Pharmacology. Accessed January 12, 2017. http://www.clinicalpharmacology-ip.com

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Minor changes to verbiage and grammar. References updated.	01.12.17	11.17

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice

current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.