Clinical Policy: Eltrombopag (Promacta)

Reference Number: PA.CP.PHAR.180
Effective Date: 01/18
Last Review Date: 04/19

Coding Implications
Revision Log

Description
Eltrombopag (Promacta®) is a thrombopoietin receptor agonist.

FDA Approved Indication(s)
Promacta is indicated for the treatment of:

- Thrombocytopenia in adult and pediatric patients 1 year and older with chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Promacta should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding.
- Thrombocytopenia in patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy. Promacta should be used only in patients with chronic hepatitis C whose degree of thrombocytopenia prevents the initiation of interferon-based therapy or limits the ability to maintain interferon-based therapy.
- Patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy
- In combination with standard immunosuppressive therapy for the first-line treatment of adults and pediatric patients 2 years and older with severe aplastic anemia.

Limitation(s) of use:

- Promacta is not indicated for the treatment of patients with myelodysplastic syndromes (MDS).
- Safety and efficacy have not been established in combination with direct-acting antiviral agents used without interferon for treatment of chronic hepatitis C infection.

Policy/Criteria
It is the policy of health plans affiliated with Pennsylvania Health and Wellness that Promacta is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Immune Thrombocytopenia (ITP) (must meet all):

1. Diagnosis of chronic ITP;
2. Prescribed by or in consultation with a hematologist;
3. Age ≥ 1 year;
4. Current (within 30 days) platelet count is < 30,000/µL or member has an active bleed;
5. Failure of systemic corticosteroids and immune globulins, unless contraindicated or clinically significant adverse effects are experienced (*see Appendix B*);
   **Prior authorization may be required for immune globulins*
6. Dose does not exceed 75 mg (1 tablet) per day.

Approval duration: 6 months

B. Chronic Hepatitis C-Associated Thrombocytopenia (must meet all):
1. Diagnosis of chronic hepatitis C-associated thrombocytopenia;
2. Prescribed by or in consultation with a hematologist, hepatologist, gastroenterologist or infectious disease specialist;
3. Age ≥ 18 years;
4. Promacta will be used concomitantly with interferon-based therapy;
5. The degree of thrombocytopenia has prevented the initiation of interferon-based therapy or limited the ability to maintain interferon-based therapy;
6. Current (within 30 days) platelet count is < 75,000/µL;
7. Dose does not exceed 100 mg (2 tablets) per day.

Approval duration: 6 months

C. Severe Aplastic Anemia (must meet all):
1. Diagnosis of severe aplastic anemia;
2. Prescribed by or in consultation with a hematologist;
3. Age ≥ 2 years;
4. For members aged 2-18 years, Promacta is prescribed in combination with immunosuppressive therapy (e.g., Atgam®, cyclosporine, cyclophosphamide);
   **Prior authorization may be required for Atgam and cyclosphosphamide*
5. Current (within 30 days) platelet count is < 50,000/µL;
6. Prescribed Dose does not exceed 150 mg (2 tablets) per day.

Approval Duration: 6 months

D. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy (*see Appendix D*);
3. Current (within the last 90 days) platelet count is < 400,000/µL;
4. For chronic hepatitis C-associated thrombocytopenia, member continues to receive interferon-based therapy;
5. If request is for a dose increase, new dose does not exceed the following :
   a. Chronic ITP: 75 mg (1 tablet) per day;
   b. Chronic hepatitis C-associated thrombocytopenia: 100 mg (2 tablets) per day;
   c. Severe aplastic anemia: 150 mg (2 tablets) daily.

Approval Duration: 6 months for hepatitis C-associated thrombocytopenia;
12 months for all other indications

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies; or

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.CP.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ANC: absolute neutrophil count
FDA: Food and Drug Administration
ITP: immune thrombocytopenia
MDS: myelodysplastic syndromes

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Corticosteroids*		
dexamethasone	**ITP** Oral dosage: *Adults*: Initially, 0.75 to 9 mg/day PO, given in 2 to 4 divided doses. Adjust according to patient response. *Children and adolescents*: 0.024 to 0.34 mg/kg/day PO or 0.66 to 10 mg/m^2/day PO, given in 2 to 4 divided doses Intramuscular or intravenous dosage: *Adults:* Initially, 0.5 to 9 mg/day IV or IM, given in 2 to 4 divided doses. Adjust according to patient response. *Children:* 0.06 to 0.3 mg/kg/day or 1.2 to 10 mg/m^2/day IV or IM in divided doses every 6 to 12 hours. Adjust according to patient response.	Dosage must be individualized and is highly variable depending on the nature and severity of the disease, route of treatment, and on patient response.
methylprednisolone	**ITP** Oral dosage: *Adults:* 4 to 48 mg/day PO in 4 divided doses. Adjust according to patient response. *Children:* 0.5 to 1.7 mg/kg/day PO in divided doses every 6 to 12 hrs Intravenous dosage: *Adults:* 10 to 40 mg IV every 4 to 6 hours for up to 72 hours *Children:* 0.11 to 1.6 mg/kg/day IV in 3 or 4 divided doses.	Dosage must be individualized and is highly variable depending on the nature and severity of the disease, route of treatment, and on patient response.
prednisone	**ITP**	Dosage must be individualized and

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Adults: Initially, 1 mg/kg PO once daily; however, lower doses of 5 mg/day to 10 mg/day PO are preferable for long-term treatment.	is highly variable depending on the nature and severity of the disease, route of treatment, and on patient response.
Immune globulins		
immune globulins (e.g., Carimune® NF, Flebogamma® DIF 10%, Gammagard® S/D, Gammaked™, Gamunex®-C, Gammaplex®, Octagam® 10%, Privigen®)	**ITP** Refer to prescribing information	Refer to prescribing information
Immunosuppressive agents*		
Atgam® (antithymocyte globulin)	**Aplastic anemia** 10 to 20 mg/kg/day IV infusion for 8 to 14 days, continuing with every-other-day dosing up to a total of 21 doses, if needed Off-label dosing: 40 mg/kg IV daily for four consecutive days in combination with cyclosporine	Varies
cyclosporine† (Sandimmune®)	**Aplastic anemia** 12 mg/kg PO daily	Varies
cyclophosphamide†	**Aplastic anemia** 45 to 50 mg/kg IV divided over 4 days	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.
Examples of corticosteroids/immunosuppressive agents provided are not all inclusive
†Off-label indication

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s): In patients with chronic hepatitis C, Promacta in combination with interferon and ribavirin may increase the risk of hepatic decompensation. Promacta may increase the risk of severe and potentially life threatening hepatotoxicity. Monitor hepatic function and discontinue dosing as recommended.

Appendix D: General Information

- Examples of positive response to therapy may include:
  - For ITP or hepatitis C-associated thrombocytopenia:
    - Increase in platelet count from baseline levels;
    - Platelet count ≥ 50,000/µL;
    - Reduction in clinically important bleeding events;
  - For aplastic anemia: any of the following hematologic responses:
    - Platelet count ≥ 50,000/µL
    - Platelet count increases to 20,000/µL above baseline or stable platelet counts with transfusion independence for a minimum of 8 weeks;
    - Hemoglobin increase > 1.5 g/dL, or a reduction of ≥ 4 units of red blood cell (RBC) transfusions for 8 consecutive weeks;
    - Absolute neutrophil count (ANC) increase of 100% or an ANC increase greater than 500/µL.

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Chronic ITP	Adults and pediatrics age ≥ 6 years: 50 mg PO QD Pediatrics age 1 to 5 years: 25 mg PO QD Dose reductions are needed for patients with hepatic impairment and some patients of East Asian ancestry. Adjust to maintain platelet count greater than or equal to 50,000/µL.	75 mg/day
Chronic hepatitis C-associated thrombocytopenia	25 mg PO QD Adjust to achieve target platelet count required to initiate antiviral therapy.	100 mg/day
Severe aplastic anemia	<u>After an insufficient response to immunosuppressive therapy:</u> 50 mg PO QD Reduce initial dose in patients with hepatic impairment or patients of East Asian ancestry. Adjust to maintain platelet count greater than 50,000/µL. <u>For first-line treatment in combination with immunosuppressive therapy:</u> Patients 12 years and older: 150 mg PO QD Patients 6 to 11 years: 75 mg PO QD Patients 2 to 5 years: 2.5 mg/kg PO QD Reduce initial dose in patients with hepatic impairment or patients of East Asian ancestry.	150 mg/day

Indication	Dosing Regimen	Maximum Dose
	Adjust to maintain platelet count greater than 50,000/µL. Total duration of treatment is 6 months.	

V. Product Availability

- Tablets: 12.5 mg, 25 mg, 50 mg, 75 mg
- Oral suspension: 12.5 mg, 25 mg

VI. References

1. Promacta Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; April 2019. Available at: https://www.us.promacta.com/. Accessed June 19, 2019.
2. Townsley DM, et al. Eltrombopag added to standard immunosuppression for aplastic anemia. N Engl J of Med. Apr 2017;376(16):1540-1550.
3. Killick SB, et al. Guidelines for the diagnosis and management of adult aplastic anemia. British Journal of Haematology, 2016, 172, 187-207.
4. Neunert C, Lim W, Crowther M, et al. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood. 2011; 117(16): 4190-4207.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: http://www.clinicalpharmacology-ip.com/. Accessed January 15, 2019.

Reviews, Revisions, and Approvals	Date	Approval Date
Added age restriction per PI. References reviewed and updated.	02/18	
Q2 2019 annual review: • **Chronic ITP: removed requirement related to splenectomy based on specialist feedback;** • **Updated limitations of use per package insert;** • **Added requirement that initial platelet counts be current (within 30 days) for all indications;** • **For cont tx approval, clarified that member must be continuing on interferon-based therapy;** • **Added MDS as a diagnosis not covered per package insert;** • **Criteria added for new FDA indication: first-line treatment of aplastic anemia in combination with standard immunosuppressive therapy;** • **Added oral suspension formulation;** • **References updated and reviewed.**	04/19	