RXADVANCE
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Clinical Policy Title:	eltrombopag
Policy Number:	RxA.457
Drug(s) Applied:	Promacta®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of business

Background

Eltrombopag (Promacta®) is a thrombopoietin receptor agonist. It is indicated for the treatment of:

Chronic ITP

- 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.

Chronic hepatitis C-associated thrombocytopenia

- 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 interferonbased therapy or limits the ability to maintain interferon-based therapy.

Severe aplastic anemia

- 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.

Myelodysplastic Syndromes (MDS) with sever Thrombocytopenia

- Thrombocytopenia in adult and older with severe MDS who are ineligible for other treatment and who are not receiving disease-modifying treatment.

Limitation(s) of use:

- Safety and efficacy have not been established in combination with direct-acting antiviral agents used without interferon for treatment of chronic hepatitis C infection.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Eltrombopag (Promacta)	Chronic ITP	Adults and pediatrics age ≥ 6 years: 50 mg PO QD Pediatrics age 1 to 5 years: 25 mg PO QD	75 mg/day

		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.	
Eltrombopag (Promacta)	Chronic hepatitis C-associated thrombocytopenia	25 mg PO QD Adjust to achieve target platelet count required to initiate antiviral therapy.	100 mg/day
Eltrombopag (Promacta)	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 once daily Reduce initial dose in patients with hepatic impairment or patients of East Asian ancestry. Adjust to maintain platelet count greater than 50,000/µL. Total duration of treatment is 6 months.	150 mg/day

Eltrombopag (Promacta)	Myelodysplastic Syndromes (MDS) with sever Thrombocytopenia	100 mg PO once daily, dose may increase in 100-mg increments at intervals of at least 2 weeks for patients with platelet counts of less than 100,000/ µL.	300 mg/day

Dosage Forms

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

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Chronic Immune Thrombocytopenia (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
Commercial: 6 months
Medicaid: 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
Commercial: 6 months
Medicaid: 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. Dose does not exceed 150 mg (2 tablets) per day.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

D. Myelodysplastic Syndromes (MDS) with sever Thrombocytopenia (must meet all):

1. Diagnosis of Myelodysplastic Syndromes (MDS) with sever Thrombocytopenia;
2. Prescribed by or in consultation with a hematologist or oncologist;
3. Age ≥ 18 year;
4. Current (within 30 days) platelet count is < 30,000/µL or member has an active bleed;
5. Dose does not exceed 300 mg (4 tablet) per day.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
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) per day;
    d. Myelodysplastic Syndromes (MDS) with severe Thrombocytopenia: 300 mg per day

Approval Duration
Commercial: Hepatitis C-associated thrombocytopenia – 6 months
All other indications: 12 months
Medicaid: Hepatitis C-associated thrombocytopenia – 6 months
All other indications: 12 months

III. Appendices

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** *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.	Dosage must be individualized and 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®, Gengraf®, Neoral®)	**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:

o 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; o 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.

References

1. Promacta Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; Revised April, 2020. Available at: https://www.us.promacta.com/. Accessed August 7, 2020.
2. Townsley DM, et al. Eltrombopag added to standard immunosuppression for aplastic anemia. N Engl J of Med. Apr 2017;376(16):1540-1550.
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4. Neunert C, Lim W, Crowther M, et al. The American Society of Hematology 2011 evidencebased 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 August 7, 2020.
6. Oliva EN, Alati C, Santini V, et al. Mediterranean Journal of Hematology and Infectious Diseases. 2018; 10(1): e2018046.
7. Promacta. Micromedex Solutions. Truven Health Analtics Inc. Greenwood Village, CO. Available at http://www.micromedexsolutions.com. Accessed August 7, 2020.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Clinical Policy Title was updated. 2. Drug(s) Applied was updated. 3. Line of Business Policy Applies to was update to all lines of business. 4. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 5. Initial Approval criteria: Commercial and Medicaid approval duration were updated from length of benefit to 6 months and added criteria for Myelodysplastic Syndromes (MDS) with sever Thrombocytopenia 6. Continued Approval criteria: Commercial and Medicaid approval duration were updated from length of benefit to 12 months and added Myelodysplastic Syndromes (MDS) with severe Thrombocytopenia: 300 mg per day 7. Updated APPENDIX B: Therapeutic Alternatives to include 2 new brands Gengraf®, Neoral® of cyclosporin. 8. Updated background to include new indication Myelodysplastic Syndromes (MDS) with sever Thrombocytopenia. 9. Updated Dosing information for Myelodysplastic Syndromes (MDS) with sever Thrombocytopenia as per clinical trials. 10. Updated Initial Approval Criteria for Myelodysplastic Syndromes (MDS) with sever Thrombocytopenia as per clinical trials. 11. References were updated. 12. Background updated to include indication: Myelodysplastic Syndromes (MDS) with sever	08/07/2020	09/14/2020

Thrombocytopenia - Thrombocytopenia in adult and older with severe MDS who are ineligible for other treatment and who are not receiving disease-modifying treatment. 13. Dosing added for Myelodysplastic Syndromes (MDS) with sever Thrombocytopenia: 100 mg PO once daily, dose may increase in 100-mg increments at intervals of at least 2 weeks for patients with platelet counts of less than 100,000/ µL. Max dosage 300 mg/day		