Clinical Policy Title:	eltrombopag
Policy Number:	RxA.457
Drug(s) Applied:	Promacta®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
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 immune thrombocytopenia (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.
  - It 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.
  - It 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.
- 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.

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.
- Promacta® is not indicated for the treatment of patients with myelodysplastic syndrome (MDS).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
eltrombopag (Promacta®)	Chronic ITP	Adults and pediatrics age ≥ 6 years: 50 mg orally once daily Pediatric age 1 to 5 years: 25 mg orally once daily Dose reductions are needed for patients with hepatic impairment and some patients of East Asian ancestry. Adjust to	75 mg/day

This clinical policy has been developed to authorize, modify, or determine coverage for individuals with similar conditions. Specific care and treatment may vary depending on individual need and benefits covered by the plan. This policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. This document may contain prescription brand name drugs that are trademarks of pharmaceutical manufacturers that are not affiliated with RxAdvance.

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Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
		maintain platelet count greater than or equal to 50,000/µL. For patients with ITP and mild, moderate, or severe hepatic impairment (Child-Pugh Class A, B, C): initiate Promacta® at a reduced dose of 25 mg once daily For patients of Asian ancestry with ITP and hepatic impairment (Child-Pugh Class A, B, C): consider initiating Promacta® at a reduced dose of 12.5 mg once daily	
eltrombopag (Promacta®)	Chronic hepatitis C-associated thrombocytopenia	25 mg orally once daily Adjust to achieve target platelet count required to initiate antiviral therapy.	100 mg/day
eltrombopag (Promacta®)	Refractory severe aplastic anemia	After an insufficient response to immunosuppressive therapy: 50 mg orally 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.	Patients 12 years and older: 150 mg orally once daily Patients 6 to 11 years: 75 mg orally once daily Patients 2 to 5 years: 2.5 mg/kg orally once daily
	First-line severe aplastic anemia	For first-line treatment in combination with immunosuppressive therapy: Patients 12 years and older: 150 mg orally once daily for 6 months Patients 6 to 11 years: 75 mg orally once daily for 6 months Patients 2 to 5 years: 2.5 mg/kg orally once daily for 6 months 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.	

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Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
		Dosage Regimen for Patients of Asian Ancestry or Those with Mild, Moderate, or Severe Hepatic Impairment (Child-Pugh Class A, B, C) in the First-Line Treatment of Severe Aplastic Anemia: Patients 12 years and older: 75 mg orally once daily for 6 months Patients 6 to 11 years: 37.5 mg orally once daily for 6 months Patients 2 to 5 years: 1.25 mg/kg orally once daily for 6 months	

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. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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 ;
   *Prior authorization may be required for immune globulins.
6. Dose does not exceed 75 mg 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;

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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 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. Promacta® is prescribed in combination with immunosuppressive therapy (e.g., Atgam®, cyclosporine, cyclophosphamide) as the first line or refractory treatment;
   *Prior authorization may be required for Atgam and cyclosphosphamide.
5. Current (within 30 days) platelet count is < 30,000/µL;
6. Request meets one of the following (a,b or c):
   a. Member is 12 years and older: 150 mg orally once daily;
   b. Member is 6 to 11 years: 75 mg orally once daily;
   c. Member is 2 to 5 years: 2.5 mg/kg orally once daily;

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has 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,b or c):
   a. Chronic ITP: 75 mg per day;
   b. Chronic hepatitis C-associated thrombocytopenia: 100 mg per day;
   c. Severe aplastic anemia: Request meets one of the following (i, ii or iii):
      i. Member is 12 years and older: 150 mg orally once daily;
      ii. Member is 6 to 11 years: 75 mg orally once daily;
      iii. Member is 2 to 5 years: 2.5 mg/kg orally once daily;

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

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

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Corticosteroids*		
dexamethasone (Active Injection D, Decadron®, Dexabliss, Dexamethasone Intensol, DoubleDex, Hemady, HiDex, MAS Care-Pak, ReadySharp Dexamethasone, TaperDex, ZCORT)	**ITP** Oral dosage: Adults: Initially, 0.75 to 9 mg/day orally, given in 2 to 4 divided doses. Adjust according to patient response. Children and adolescents: 0.024 to 0.34 mg/kg/day orally or 0.66 to 10 mg/m^2/day orally, 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 intravenous or intramuscular 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 (DEPO-Medrol®, Medrol®, SOLU-Medrol)	**ITP** Oral dosage: Adults: 4 to 48 mg/day orally in 4 divided doses. Adjust according to patient response. Children: 0.5 to 1.7 mg/kg/day orally in divided doses every 6 to 12 hrs. Intravenous dosage: Adults: 10 to 40 mg intravenous every 4 to 6 hours for up to 72 hours. Children: 0.11 to 1.6 mg/kg/day intravenous 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.

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Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Prednisone (predniSONE Intensol™, Rayos)	**ITP** Adults: Initially, 1 mg/kg orally once daily; however, lower doses of 5 mg/day to 10 mg/day orally 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 globulin: e.g. Flebogamma® DIF 10%, Gamunex®C, Gammaked™ Gammaplex®, Privigen® Octagam® 10%)	**ITP** Refer to prescribing information	Refer to prescribing information
Immunosuppressive agents*		
antithymocyte globulin : Atgam®	**Aplastic anemia** 10 to 20 mg/kg/day intravenous 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 intravenous daily for four consecutive days in combination with cyclosporine	Varies
cyclosporine† (Sandimmune®, Gengraf®, Neoral®)	**Aplastic anemia** 12 mg/kg orally once daily	Varies
cyclophosphamide†	**Aplastic anemia** 45 to 50 mg/kg intravenous divided over 4 days	Varies

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

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- 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.

References

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5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021 Available at: https://www.clinicalkey.com/pharmacology/ . Accessed July 8, 2021.
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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	08/07/2020	09/14/2020

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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 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.		
Policy was reviewed: 1. Background was updated to remove indication “Myelodysplatic Syndromes (MDS) with severe Thrombocytopenia”. 2. Background was updated to include Limitation(s) of Use “Promacta® is not indicated for the treatment of patients with myelodysplastic syndrome (MDS).”. 3. Dosing Information dosing regimen was updated to include hepatic impairment dosing for indication Chronic ITP, “For	07/08/2021	09/14/2021

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patients with ITP and mild, moderate, or severe hepatic impairment (Child-Pugh Class A, B, C)…" and "For patients of Asian ancestry with ITP and hepatic impairment (Child-Pugh Class A, B, C)…". 4. Dosing Information was updated to include new indication as an addition to existing indication refractory severe aplastic anemia, "first-line severe aplastic anemia." 5. Dosing Information maximum dose for indications Refractory Severe Aplastic Anemia and First-Line Severe Aplastic Anemia was updated to include "Patients 12 years and older: 150 mg orally once daily; Patients 6 to 11 years: 75 mg…". 6. Dosing Information dosing regimen for indications Refractory Severe Aplastic Anemia and First-Line Severe Aplastic Anemia was updated to include "Dosage Regimen for Patients of Asian Ancestry or Those with Mild, Moderate, or Severe Hepatic Impairment (Child-Pugh Class A, B, C) in the First-Line Treatment of Severe Aplastic Anemia…". 7. Dosing Information was updated to remove indication, "Myelodysplatic Syndromes (MDS) with severe Thrombocytopenia" and its subsequent dosing regimen and maximum dose. 8. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 9. Initial approval criteria I.C.4 was updated to include "…as the first line or refractory treatment;". 10. Initial Approval Criteria I.C.5 was updated to remove "Member with Mild, Moderate, or Severe Hepatric Impairment…". 11. Initial Approval Criteria I.C.6. was updated to include recommended dose for " Severe aplastic anemia: Member is 12 years and older: 150 mg orally once daily; Member is 6 to 11 years: 75 mg orally once daily;..". 12. Initial Approval Criteria I.D was updated to remove indication , "Myelodysplatic Syndromes (MDS) with severe Thrombocytopenia." 13. Continued Therapy Approval Criteria II.A.1.		

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was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 14. Continued Therapy Approval Criteria II.A.4 was updated to remove “Member with Mild, Moderate, or Severe Hepatic Impairment…”. 15. Continued Therapy Approval Criteria II.A.5.d was updated to remove indication “Myelodysplatic Syndromes (MDS) with severe Thrombocytopenia.” 16. Continued Therapy Approval Criteria II.A.5.c. was updated to include recommended dose for “Severe aplastic anemia: Member is 12 years and older: 150 mg orally once daily; Member is 6 to 11 years: 75 mg orally once daily; Member is 2 to 5 years: 2.5 mg/kg orally once daily…”. 17. Appendix A was updated to remove abbreviation MDS. 18. Therapeutic Alternatives verbiage was updated to “Below are suggested therapeutic alternatives based on clinical guidance..”. 19. Appendix B: Therapeutic Alternatives drug name was updated to include drugs “Active Injection D, Decadron®, Dexabliss, Dexamethasone Intensol, DoubleDex, Hemady, HiDex, MAS Care-Pak, ReadySharp Dexamethasone, TaperDex, ZCORT”, “DEPO-Medrol®, Medrol®, SOLU-Medrol”, and “predniSONE Intensol™, Rayos”. 20. Appendix B: Therapeutic Alternatives drug name was updated to remove unavailable/inactive drugs Carimune NF and Gammagard. 21. Statement about drug listing format in Appendix B is updated to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 22. References were reviewed and updated.		

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