Clinical Policy Title:	Thrombopoetin (TPO) Receptor Agonists and Antihemmorhagic Agents
Policy Number:	RxA.457
Drug(s) Applied:	Promacta®, Doptelet®, Tavalisse®
Original Policy Date:	03/06/2020
Last Review Date:	8/27/2024
Line of Business Policy Applies to:	All lines of business (except Medicare)

Criteria

I. Initial Approval Criteria

A. Persistent or Chronic Immune Thrombocytopenia (must meet all)**:**

1. One of the following (a or b):
    a. Diagnosis of persistent or chronic ITP and the request is for Doptelet, Promacta, or Tavalisse;
    b. Diagnosis of persistent, relapsed, or refractory ITP and the request is for Promacta;
2. Member must meet one of the following (a or b):
    a. Baseline platelet count is less than 30,000/µL within the past 30 days;
    b. Member has an active bleed;
3. Member meets one of the following (a or b):
    a. Trial and failure of systemic corticosteroids, rituximab, and immune globulins, unless contraindicated or clinically significant adverse effects are experienced;
    b. Member has undergone a splenectomy.

Approval Duration
All Lines of Business (except Medicare): 12 months

B. Chronic Hepatitis C-Associated Thrombocytopenia (must meet all)**:**

1. Diagnosis of chronic hepatitis C-associated thrombocytopenia;
2. The request is for Promacta;
3. Promacta® will be used concomitantly with an interferon-based therapy;
4. Baseline platelet count is less than 75,000/µL within the past 30 days;

Approval Duration
All Lines of Business (except Medicare): 12 months

C. Severe Aplastic Anemia (must meet all)**:**

1. Diagnosis of severe aplastic anemia;
2. The request is for Promacta;
3. The request is prescribed in one of the following ways (a or b):
    a. First line therapy in combination with an immunosuppressive therapy (e.g., Atgam®, cyclosporine, cyclophosphamide);
    b. Refractory or second-line therapy as a single agent following insufficient response to immunosuppressive therapy (e.g., Atgam, cyclosporine, cyclophosphamide);

4. Baseline platelet count is less than 30,000/µL within the past 30 days;

Approval Duration

All Lines of Business (except Medicare): 12 months

D. Thrombocytopenia with Chronic Liver Disease (must meet all)**:**

1. Diagnosis of chronic liver disease;
2. The request is for Doptelet;
3. Platelet count is less than 50,000/µL within the past 14 days;
4. Member is scheduled to undergo a procedure within the next 30 days.

Approval duration

All Lines of Business (except Medicare): 14 days

II. Continued Therapy Approval

A. Persistent or Chronic Immune Thrombocytopenia (must meet all)**:**

1. Auto-approval based on lookback functionality within the past 120 days as a proxy for member responding positively to therapy.
2.

Approval duration

All Lines of Business (except Medicare): 12 months

B. Chronic Hepatitis-C Associated Thrombocytopenia (must meet all)**:**

1. Auto-approval based on lookback functionality within the past 120 days as a proxy for member responding positively to therapy.
2. Member continues to receive an interferon-based therapy.

Approval duration

All Lines of Business (except Medicare): 12 months

C. Severe Aplastic Anemia (must meet all)**:**

1. Auto-approval based on lookback functionality within the past 120 days as a proxy for member responding positively to therapy.

Approval duration

All Lines of Business (except Medicare): 12 months

D. Thrombocytopenia with Chronic Liver Disease (must meet all)**:**

1. Re-authorization is not permitted. Members must meet the initial approval criteria.

Approval duration

All Lines of Business (except Medicare): Not applicable

References

1. Townsley DM, Scheinberg P, Winkler T, et al. Eltrombopag added to standard immunosuppression for aplastic anemia. N Engl J of Med. Apr 2017;376(16):1540-1550. Available at: https://www.nejm.org/doi/full/10.1056/nejmoa1613878 . Accessed April 26, 2023.
2. National Comprehensive Cancer Network. Myelodysplastic Syndromes Version 1. 2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed April 26, 2023.

3. Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Advances*. 2019;3(23):3829-3866.Available at: https://ashpublications.org/bloodadvances/article/3/23/3829/429213/American-Society-of-Hematology-2019-guidelines-for. Accessed August 27th, 2024.
4. Kumar A, Mhaskar R, Grossman BJ, et al on behalf of the AABB (American Association of Blood Banks) Platelet Transfusion Guidelines Panel. Platelet transfusion: a systematic review of the clinical evidence. Transfusion. 2015; 55: 1116-1127. Available at: https://pubmed.ncbi.nlm.nih.gov/25387589/. Accessed December 27, 2022.
5. Hayashi H, Beppu T, Shirabe K, Maehara Y, and Baba H. Management of thrombocytopenia due to liver cirrhosis: a review. World J Gastroenterol. 2014; 20(10): 2595-2605. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3949268/. Accessed December 27, 2022.
6. Bussel J, Arnold DM, Grossbard E, et al. Fostamatinib for the treatment of adult persistent and chronic immune thrombocytopenia: Results of two phase 3, randomized, placebo-controlled trials. American Journal of Hematology. 2018;93(7):921-930. Available at: ericanHYPERLINK "https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6055608/" Journal of April 9, 2024. Hematology. 2018;93(7):921-930. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6055608/. Accessed April 9, 2024.

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. References were updated.	08/07/2020	09/14/2020
Policy was reviewed: 1. Initial approval criteria I.C.4 was updated to include "…as the first line or refractory treatment;". 2. Initial Approval Criteria I.C.5 was updated to remove "Member with Mild, Moderate, or Severe Hepatric Impairment…". 3. Initial Approval Criteria I.C.6. was updated to include recommended dose for " Severe	07/08/2021	09/14/2021

aplastic anemia: Member is 12 years and older: 150 mg orally once daily; Member is 6 to 11 years: 75 mg orally once daily;..". 4. Initial Approval Criteria I.D was updated to remove indication , "Myelodysplatic Syndromes (MDS) with severe Thrombocytopenia." 5. Continued Therapy Approval Criteria II.A.1. was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 6. Continued Therapy Approval Criteria II.A.4 was updated to remove "Member with Mild, Moderate, or Severe Hepatic Impairment…". 7. Continued Therapy Approval Criteria II.A.5.d was updated to remove indication "Myelodysplatic Syndromes (MDS) with severe Thrombocytopenia." 8. 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…". 9. References were reviewed and updated.		
Policy was reviewed: 1. Initial Approval Criteria, I.A.1: Updated indication from Diagnosis of chronic ITP to Diagnosis of persistent or chronic ITP. 2. Initial Approval Criteria, I.A.5: Updated to include new combination therapy criteria Promacta® is not prescribed concurrently with rituximab or another thrombopoietin receptor agonist (e.g., Doptelet®, Nplate®). 3. Initial Approval Criteria, I.C.4: Updated combination therapy criteria from 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 to Promacta® is prescribed for one (1) of the following (a or b): a. As first line therapy in combination with immunosuppressive therapy (e.g.,	03/29/2022	07/18/2022

Atgam®, cyclosporine, cyclophosphamide); b. Refractory or second-line treatment as a single agent following insufficient response to immunosuppressive therapy (e.g., Atgam, cyclosporine, cyclophosphamide). 4. Initial Approval Criteria, I.C.6.b: Updated to include new dosing criteria for indication Refractory severe aplastic anemia. 5. Initial Approval Criteria, I.D: Updated to include approval criteria for indication, Myelodysplastic Syndromes. 6. Continued Therapy Approval, II.A.5: Updated to include new combination therapy criteria for persistent or chronic ITP: Promacta® is not prescribed concurrently with rituximab or another thrombopoietin receptor agonist (e.g., Doptelet, Nplate). 7. Continued Therapy Approval, II.A.6.a: Updated indication from chronic ITP: 75 mg per day to Persistent or chronic ITP: 75 mg per day. 8. Continued Therapy Approval, II.A.6.c: Updated to include new dosing criteria for indication Refractory severe aplastic anemia. 9. Continued Therapy Approval Criteria, II.B: Updated to include approval criteria for indication, Myelodysplastic Syndromes. 10. References were reviewed and updated.		
Policy was reviewed: 1. Initial Approval Criteria: Approval duration updated from 6 months to 12 months. 2. Initial Approval Criteria I.B.5: Updated to remove that the degree of thrombocytopenia has prevented the initiation of interferon-based therapy or limited the ability to maintain interferon-based therapy. 3. Initial Approval Criteria, I.D.4.b and I.D.4.c: Updated to include new criteria pertaining to indication Myelodysplastic Syndromes, b. Member has thrombocytopenia or neutropenia and one of the following (i, ii, iii, or iv): i. Age ≤ 60 years with ≤ 5% marrow blasts;	04/26/2023	07/13/2023

ii. Hypocellular marrows; iii. Paroxysmal nocturnal hemoglobinuria (PNH) clone positivity; iv. STAT-3 mutant cytotoxic T-cell clones; c. Member has symptomatic anemia with all the following (i, ii, and iii): i. No del(5q); ii. Serum erythropoietin > 500 mU/mL; iii. Good probability to respond to immunosuppressive therapy; 4. References were reviewed and updated.		
Policy was reviewed.	10/19/2023	10/19/2023
Policy was reviewed: 1. Consolidated policies for Promacta, Doptelet, and Tavalisse. 2. Removed Mulpleta from consolidation because it is non-formulary. 3. Removed age, specialist, and dosing. 4. Removed off-label indication. 5. Removed duplication therapy. 6. Consolidated and updated references.	08/27/2024	09/12/2024