Clinical Policy: Avatrombopag (Doptelet)

Reference Number: ERX.SPA.288
Effective Date: 12.01.18
Last Review Date: 11.21
Line of Business: Commercial, Medicaid

Revision Log

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

Description
Avatrombopag (Doptelet®) is a thrombopoietin (TPO) receptor agonist.

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

- Thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure.
- Thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.

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

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Doptelet is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of chronic liver disease;
2. Prescribed by or in consultation with a hematologist, hepatologist, or gastroenterologist;
3. Age ≥ 18 years;
4. Recent (within the past 14 days) platelet count is < 50 x 10^9/L;
5. For members with platelet count < 40 x 10^9/L, failure of Mulpleta®, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for Mulpleta*
6. Member is scheduled to undergo a medical or dental procedure within the next 30 days;
7. Dose does not exceed (a or b):
   a. Platelet count < 40 x 10^9/L: 60 mg (3 tablets) per day for a total of 5 days;
   b. Platelet count of 40 to < 50 x 10^9/L: 40 mg (2 tablets) per day for a total of 5 days.

Approval duration: 14 days (no more than 5 total days of treatment)

B. Chronic Immune Thrombocytopenia (must meet all)**:**

1. Diagnosis of chronic ITP;
2. Prescribed by or in consultation with a hematologist;
3. Age ≥ 18 years;
4. Current (within 30 days) platelet count < 30,000/µL or member has an active bleed;
5. Member meets one of the following (a or b):
   a. Failure of a systemic corticosteroid;
   b. Member has an intolerance or contraindication to systemic corticosteroids, and failure of an immune globulin, unless contraindicated or clinically significant adverse effects are experienced *(see Appendix B)*;
   **Prior authorization may be required for immune globulins*

6. Doptelet is not prescribed concurrently with rituximab or another thrombopoietin receptor agonist (e.g., Promacta®, Nplate®);
7. Dose does not exceed 40 mg (2 tablets) per day.

Approval duration: 6 months

C. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Thrombocytopenia with Chronic Liver Disease

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

Approval duration: Not applicable

B. Chronic Immune Thrombocytopenia (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy (e.g., increase in platelet count from baseline, reduction in bleeding events);
3. Doptelet is not prescribed concurrently with rituximab or another thrombopoietin receptor agonist (e.g., Promacta, Nplate);
4. If request is for a dose increase, new dose does not exceed 40 mg (2 tablets) per day.

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 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 – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ASH: American Society of Hematology
FDA: Food and Drug Administration
ITP: immune thrombocytopenia
TPO: thrombopoietin

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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Thrombocytopenia with chronic liver disease		
Mulpleta® (lusutrombopag)	3 mg PO QD for a total of 7 days	3 mg/day
Chronic immune thrombocytopenia*		
Corticosteroids		
dexamethasone	Oral dosage: Initially, 0.75 to 9 mg/day PO in 2 to 4 divided doses. Adjust according to patient response Intramuscular or intravenous dosage:	Highly variable depending on the nature and severity of the disease, route of

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Initially, 0.5 to 9 mg/day IV or IM in 2 to 4 divided doses. Adjust according to patient response	treatment, and on patient response
methylprednisolone	10-40 mg IV every 4-6 hours for up to 72 hours	
prednisone	Initially, 1 mg/kg PO QD; however, lower doses of 5 mg/day to 10 mg/day PO are preferable for long-term treatment	
Immune globulins		
Immune globulins (e.g., Carimune® NF, Flebogamma® DIF 10%, Gammagard® S/D, Gammaked™, Gamunex®-C, Gammaplex®, Octagam® 10%, Privigen®, etc.)	Refer to prescribing information	Refer to prescribing information

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*

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information
- Examples of chronic liver disease include: alcoholic liver disease, chronic viral hepatitis (e.g., hepatitis B and C), and nonalcoholic steatohepatitis.
- Definitions of acute v. chronic ITP:
  - Per an International Working Group consensus panel of ITP experts, ITP is defined as newly diagnosed (diagnosis to 3 months), persistent (3 to 12 months from diagnosis), or chronic (lasting for more than 12 months). Although not formally validated, these definitions are supported and used by the American Society of Hematology (ASH).
- Per the 2019 ASH guidelines, response to treatment was defined by the following:
  - A response is defined as a platelet count ≥ 30,000/μL and a greater than 2-fold increase in platelet count from baseline measured on 2 occasions > 7 days apart and the absence of bleeding.
  - A failure would be defined as a platelet count < 30,000/μL or a less than 2-fold increase in platelet count from baseline or the presence of bleeding. Platelet count must be measured on 2 occasions more than a day apart.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Thrombocytopenia with chronic liver disease	Platelet count < 40 x 10^9/L: 60 mg PO QD for a total of 5 days Platelet count of 40 to < 50 x 10^9/L: 40 mg PO QD for a total of 5 days	See regimen
Chronic ITP	Initiate at 20 mg PO QD and titrate to maintain platelet count ≥ 50 x 10^9/L	40 mg/day

VI. Product Availability
Tablet: 20 mg

VII. References

1. Doptelet Prescribing Information. Durham, NC: Dova Pharmaceuticals, Inc.; August 2020. Available at: https://www.doptelet.com. Accessed July 21, 2021.
2. 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.
3. 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.
4. Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Adv. 2019; (3)23:3829-3866.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at: http://www.clinicalpharmacology-ip.com/.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	07.17.18	11.18
4Q 2019 annual review: criteria added for new FDA indication: chronic immune thrombocytopenia; references reviewed and updated.	08.13.19	11.19
Added requirement that Doptelet is not prescribed concurrently with rituximab or another thrombopoietin receptor agonist for ITP; revised systemic corticosteroid and immune globulin trial to tiered re-direction with immune globulin trial only if corticosteroid cannot be used per ASH 2011 guideline and specialist feedback.	05.19.20	08.20
4Q 2020 annual review: added redirections to Mulpleta for thrombocytopenia in chronic liver disease and to Promacta for chronic ITP per current formulary status; references reviewed and updated.	08.02.20	11.20
4Q 2021 annual review: removed redirection to Promacta as this product is non-formulary; references reviewed and updated.	07.21.21	11.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.