Clinical Policy Title:	avatrombopag
Policy Number:	RxA.362
Drug(s) Applied:	Doptelet®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

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

It 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
avatrombopag (Doptelet®)	Thrombocytopenia with chronic liver disease	Platelet count < 40 x 10^9/L: 60 mg orally once daily for a total of 5 days Platelet count of 40 to < 50 x 10^9/L: 40 mg orally once daily for a total of 5 days	See regimen
	Chronic ITP	Initiate at 20 mg orally once daily and titrate to 40 mg/day to maintain platelet count ≥ 50 x10^9/L	40 mg/day

Dosage Forms

- Tablets: 20 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. 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 lusutrombopag (Mulpleta®) unless contraindicated or clinically significant adverse effects are experienced;
   *Prior authorization may be required for lusutrombopag (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
Commercial: 14 days (no more than 5 total days of treatment)
Medicaid: 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. Failure of systemic corticosteroids and immune globulins at up to maximally indicated doses, 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 40 mg (2 tablets) per day.

Approval duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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. 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 (e.g., increase in platelet count from baseline, reduction in bleeding events);
3. If request is for a dose increase, new dose does not exceed 40 mg (2 tablets) per day.

Approval duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
ASH: American Society of Hematology
FDA: Food and Drug Administration
ITP: Immune Thrombocytopenia
TPO: Thrombopoietin

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
Thrombocytopenia with chronic liver disease		
Mulpleta® (lusutrombopag)	3 mg orally once daily for a total of 7 days	3 mg/day
Chronic immune thrombocytopenia*		
Corticosteroids		
dexamethasone	Oral dosage: Initially, 0.75 to 9 mg/day orally in 2 to 4 divided doses. Adjust according to patient response Intramuscular or intravenous dosage: Initially, 0.5 to 9 mg/day intravenously or intramuscularly in 2 to 4 divided doses. Adjust according to patient response	Highly variable depending on the nature and severity of the disease, route of treatment, and on patient response
methylprednisolone	10-40 mg intravenously every 4-6 hours for up to 72 hours	
prednisone	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	
Immune globulins		
Immune globulins (e.g.,Flebogamma® DIF 10%, Gammaked™, Gamunex®-C, Gammaplex®, Octagam® 10%, Privigen®, etc.)	Refer to prescribing information	Refer to prescribing information

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.

- Boxed warning(s):
  - 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 vs. 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 2011 ASH guidelines, response to treatment was defined by the following:
  - A response would be 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.

References

1. Doptelet Prescribing Information. Durham, NC: Dova Pharmaceuticals, Inc.; October 2020. Available at: https://www.doptelet.com. Accessed May 31, 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. Accessed May 31, 2021.
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. Accessed May 31, 2021.
4. Neunert C, Lim W, Crowther M, Cohen A, Solberg L, and Crowther MA. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood. 2011; 117(16): 4190-4207. https://doi.org/10.1182/blood-2010-08-302984. Accessed May 31, 2021.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/. Accessed May 31, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established	01/2020	03/06/2020
Policy was reviewed. 1) Background info updated. 2) Clinical policy (initial approval criteria & continued therapy approval) was updated. 3) Appendices updated. 4) References were updated.	06/28/2020	09/14/2020
Policy was reviewed: 1) Statement about provider sample "The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 2) Dosing Information for Chronic Immune thrombocytopenia (ITP) was updated to include, "and titrate to 40 mg/day." 3) Continued Therapy Approval	05/31/2021	09/14/2021

Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 4) Therapeutic Alternatives verbiage was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance..". 5) Appendix B was updated to remove drug names “Carimune® NF” and “Gammagard® S/D.” 6) Statement about drug listing format in Appendix B is rephrased 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". 7) References were reviewed and updated.		