

Clinical Policy: Avatrombopag (Doptelet)

Reference Number: CP.PHAR.130

Effective Date: 07.17.18

Last Review Date: 11.19

Line of Business: Commercial, HIM, 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.

It is the policy of health plans affiliated with Centene Corporation[®] 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 \geq 18 years;
4. Recent (within the past 14 days) platelet count is $< 50 \times 10^9/L$;
5. For members with platelet count $< 40 \times 10^9/L$, 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 $< 40 \times 10^9/L$: 60 mg (3 tablets) per day for a total of 5 days;
 - b. Platelet count of 40 to $< 50 \times 10^9/L$: 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 \geq 18 years;
4. Current (within 30 days) platelet count $<$ 30,000/ μ L 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: 6 months

C. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 Centene benefit 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. 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 Centene benefit and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid 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 for all relevant lines of business 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: Initially, 0.5 to 9 mg/day IV or IM 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 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 2011 ASH guidelines, response to treatment was defined by the following:
 - A response would be defined as a platelet count $\geq 30,000/\mu\text{L}$ 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 $< 30,000/\mu\text{L}$ 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 $< 40 \times 10^9/\text{L}$: 60 mg PO QD for a total of 5 days Platelet count of 40 to $< 50 \times 10^9/\text{L}$: 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 $\geq 50 \times 10^9/\text{L}$	40 mg/day

VI. Product Availability

Tablet: 20 mg

VII. References

1. Doptelet Prescribing Information. Durham, NC: Dova Pharmaceuticals, Inc.; June 2019. Available at: <https://www.doptelet.com>. Accessed July 9, 2019.
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, 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. Accessed July 8, 2019. <https://doi.org/10.1182/blood-2010-08-302984>.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: <http://www.clinicalpharmacology-ip.com/>.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	07.17.18	11.18
Added HIM line of business; added requirement for trial of Mulpleta if platelet count is < 40 x 10 ⁹ /L per SDC and existing clinical guidance.	03.04.19	
4Q 2019 annual review: criteria added for new FDA indication: chronic immune thrombocytopenia; references reviewed and updated.	08.13.19	11.19

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the non-formulary policy; HIM.PA.103.

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