Original Effective Date: 05/2019
Current Effective Date: 12/28/2025
Last P&T Approval/Version: 10/29/2025
Next Review Due By: 07/2026
Policy Number: C16445-A

Doptelet (avatrombopag)

PRODUCTS AFFECTED

Doptelet (avatrombopag)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Chronic liver disease-associated thrombocytopenia, Chronic immune thrombocytopenia (CITP)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

FOR ALL INDICATIONS:

1. Doptelet (avatrombopag) is NOT being used concurrently with another thrombopoietic agent or spleen tyrosine kinase inhibitor [e.g., eltrombopag, Nplate (romiplostim), Mulpleta (lusutrombopag), or Tavalisse (fostamatinib)]

AND

2. Prescriber attests or clinical reviewer has found the medication is NOT being used to normalize platelet counts
   AND
3. IF THIS IS A NON-FORMULARY/NON-PREFERRED PRODUCT: Documentation of trial/failure of or serious side effects to a majority (not more than 3) of the preferred formulary PDL alternatives for the given diagnosis. Submit documentation including medication(s) tried, dates of trial(s) and reason for treatment failure(s).

A. THROMBOCYTOPENIA IN CHRONIC LIVER DISEASE (TICL):

1. Documented diagnosis of chronic liver disease-associated thrombocytopenia
   AND
2. The member is scheduled to undergo a procedure (excluding members undergoing neurosurgical interventions, thoracotomy, laparotomy, or organ resection)
   AND
3. The medication is being initiated 10 to 13 days prior to the scheduled procedure AND the member is undergoing the procedure 5 to 8 days after the last dose
   AND
4. Documentation the member has a platelet count <50 x10^9/L within the past 30 days [DOCUMENTATION REQUIRED]

B. CHRONIC IMMUNE THROMBOCYTOPENIA (ITP):

1. Documented diagnosis of chronic immune thrombocytopenia (ITP)
   AND
2. Documentation that member meets ONE of the following [DOCUMENTATION REQUIRED]:
   a) Platelet count less than 20 x 10^9/L (20,000/mm^3)
      OR
   b) Platelet count less than 30 x 10^9/L with ITP whose degree of thrombocytopenia and clinical condition(s) increase the risk of bleeding (e.g., hypertension, renal insufficiency, concomitant antiplatelet agents or anticoagulant medications, alcoholism, infections, undergoing a medical or dental procedure with blood loss anticipation, recent surgery, head trauma, pediatric age)
   AND
3. Documented failure, serious side effects, or contraindication to at least ONE of the following ITP treatments:
   a) Corticosteroids (i.e., prednisone, methylprednisolone, dexamethasone) at immunosuppressive doses (See Appendix), OR
   b) Intravenous immune globulin (IVIG), OR
   c) Immunosuppressive therapy (i.e., cyclosporine, mycophenolate mofetil, sirolimus), OR
   d) Has had splenectomy or is not a surgery candidate

CONTINUATION OF THERAPY:

A. THROMBOCYTOPENIA IN CHRONIC LIVER DISEASE (TICL): N/A

B. CHRONIC IMMUNE THROMBOCYTOPENIA (CITP):

1. Documentation of positive clinical response to therapy as evidenced by increase in platelet count to a level sufficient to avoid clinically important bleeding, OR increase or achievement of platelet count to 50 x 10^9/L or greater [DOCUMENTATION REQUIRED]
   NOTE: Per the FDA label, discontinue Doptelet if the platelet count does not increase to greater than or equal to 50×109 /L after 4 weeks of dosing at the maximum dose
   AND
2. Prescriber attests member still requires avatrombopag (Doptelet) to maintain a platelet count sufficient to avoid clinically important bleeding
   AND

3. Prescriber attests or clinical reviewer has found member does not have any intolerable adverse effects or drug toxicity
   AND
4. Adherence to therapy at least 85% of the time as verified by Prescriber and member's medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation

DURATION OF APPROVAL:
TICL: Initial authorization: 5 days, Continuation of therapy: N/A
CITP: Initial authorization: 3 months, Continuation of therapy: 12 months
MOLINA REVIEWER NOTE: For Texas Marketplace, please see Appendix.

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a hematologist, or physician specializing in the treatment of thrombocytopenia in patients with chronic ITP, hepatologist, or surgeon. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization (for CITP) requests]

AGE RESTRICTIONS:
TICL: 18 years of age and older
CITP: 1 year of age and older

QUANTITY:
TICL: Platelet count 40 to <50 x10^9/L – 40 mg (2 tablets) once daily for 5 consecutive days
TICL: Platelet count <40 x10^9/L – 60 mg (3 tablets) once daily for 5 consecutive days
CITP:
Adults and patients 6 years of age and older: 20 mg once daily; Dose can be adjusted or frequency of dosing to maintain platelet count greater than or equal to 50 $x10^9$ /L. Do not exceed 40 mg per day.
Pediatric patients 1 year to less than 6 years of age: 10 mg sprinkle once daily; Dose can be adjusted or frequency of dosing to maintain platelet count greater than or equal to 50 $x10^9$ /L. Do not exceed 20 mg per day.

Maximum Quantity Limits
TICL: 60 mg daily for 5 days
CITP: 40 mg daily, 20 mg sprinkle daily

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Thrombopoietin (TPO) Receptor Agonist

FDA-APPROVED USES:
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 who have had an insufficient response to a previous treatment
- Thrombocytopenia in pediatric patients 1 year and older with persistent or chronic immune

thrombocytopenia who have had an insufficient response to a previous treatment

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
Reserved for State specific information. *Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*

State Specific Information
State Marketplace
Texas (Source: Texas Statutes, Insurance Code)
"Sec. 1369.654. PROHIBITION ON MULTIPLE PRIOR AUTHORIZATIONS.
(a) A health benefit plan issuer that provides prescription drug benefits *may not require an enrollee to receive more than one prior authorization annually* of the prescription drug benefit for *a prescription drug prescribed to treat an autoimmune disease, hemophilia, or Von Willebrand disease*.
(b) This section does not apply to:
(1) opioids, benzodiazepines, barbiturates, or carisoprodol;
(2) prescription drugs that have a typical treatment period of less than 12 months;
(3) drugs that:
(A) have a boxed warning assigned by the United States Food and Drug Administration for use; and
(B) must have specific provider assessment; or
(4) the use of a drug approved for use by the United States Food and Drug Administration in a manner other than the approved use."

APPENDIX 1:
Systemic corticosteroid immunosuppressive doses include:
≥ 14 days therapy with doses ≥ 80 mg per day of prednisone.
Equivalent doses include:
- ≥ 400mg/day cortisone
- 320mg/day hydrocortisone
- 80mg/day prednisolone
- 64mg/day methylprednisolone
- 12mg/day dexamethasone

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Doptelet is a small molecule TPO receptor agonist that stimulates proliferation and differentiation of megakaryocytes from bone marrow progenitor cells, resulting in an increased platelet production. It is administered orally as a tablet and is indicated for the treatment of thrombocytopenia in adult members with chronic liver disease who are scheduled to undergo a procedure.
Efficacy
The efficacy of Doptelet for the treatment of thrombocytopenia in members with chronic liver disease who are scheduled to undergo a procedure was established in 2 identically-designed multicenter, randomized, double-blind, placebo-controlled trials (ADAPT-1 (NCT01972529) and ADAPT-2 (NCT01976104)). In each study, members were assigned to the Low Baseline Platelet Count Cohort (40 x10 L) or the High Baseline Platelet Count Cohort (≥40 to 50 x10^9 L) based on their platelet count at Baseline. Members were then randomized in a 2:1 ratio to either Doptelet or placebo. Members were stratified according to hepatocellular cancer (HCC) status and risk of bleeding associated with the elective procedure (low, moderate, or high). Members undergoing neurosurgical interventions, thoracotomy, laparotomy or organ resection were not eligible for enrollment. Members in the Low Baseline Platelet

Count Cohort received 60 mg Doptelet or matching placebo once daily for 5 days, and members in the High Baseline Platelet Count Cohort received 40 mg Doptelet or matching placebo once daily for 5 days. Eligible members were scheduled to undergo their procedure (low, moderate, or high bleeding risk) 5 to 8 days after their last dose of treatment. Member populations were similar between the pooled Low and High Baseline Platelet Count Cohorts and consisted of 66% male and 35% female; median age 58 years and 61% White, 34% Asian, and 3% Black. In ADAPT-1, a total of 231 members were randomized, 149 members were treated with Doptelet and 82 members were treated with placebo. In the Low Baseline Platelet Count Cohort, the mean Baseline platelet count for the Doptelet-treated group was 31.1 x10^9 /L and for placebo- treated s 30.7 x10 /L. In the High Baseline Platelet Count Cohort, the mean Baseline platelet count for the Doptelet-treated members was 44.3 x10^9 /L and for placebo-treated members was 44.9 x10 /L. In ADAPT-2, a total of 204 members were randomized, 128 members were treated with Doptelet and 76 members were treated with placebo. In the Low Baseline Platelet Count Cohort, the mean Baseline platelet count for the Doptelet-treated group was 32.7 x10^9/L and for placebo-treated members was 32.5 x10 /L. In the High Baseline Platelet Count Cohort, the mean Baseline platelet count for the Doptelet- treated members was 44.3 x10^9/L and for placebo-treated members was 44.5 x10^9/L. Across both baseline platelet count cohorts and the avatrombopag and placebo treatment groups, members underwent a broad spectrum of types of scheduled procedures that ranged from low to high bleeding risk. The major efficacy outcome was the proportion of members who did not require a platelet transfusion or any rescue procedure for bleeding after randomization and up to 7 days following an elective procedure. Responders were defined as members who did not require a platelet transfusion or any rescue procedure for bleeding after randomization and up to 7 days following a scheduled procedure. In both baseline platelet count cohorts, members in the Doptelet treatment groups had a greater proportion of responders than the corresponding placebo treatment groups that was both clinically meaningful and statistically significant. In members in the Low Baseline Platelet Count Cohort, the proportion of subjects not requiring a platelet transfusion or any rescue procedure for bleeding was 66% (n=90) for Doptelet 60 mg in ADAPT-1 and 69% (n=70) in ADAPT-2. In members in the High Baseline Platelet Count Cohort, the proportion of subjects not requiring a platelet- transfusion or any rescue procedure for bleeding was 88% (n=59) for Doptelet 40 mg and 88% (n=58) in ADAPT-2. Safety The safety of Doptelet was evaluated in two international, identically designed, randomized, double-blind, placebo-controlled trials, ADAPT-1 and ADAPT-2, in which 430 members with chronic liver disease and thrombocytopenia received either Doptelet (n=274) or placebo (n=156) daily for 5 days prior to a scheduled procedure, and had 1 post-dose safety assessment. Members were divided into two groups based on their mean platelet count at baseline: -Low Baseline Platelet Count Cohort (less than 40 x10^9/L) who received Doptelet 60 mg once daily for 5 days -High Baseline Platelet Count Cohort (40 to less than 50 x10^9 / L) who received Doptelet 40 mg once daily for 5 days The majority of members were males (65%) and median subject age was 58 years (ranging from 19- 86 years of age). The racial and ethnic distribution was White (60%), Asian (33%), Black (3%), and Other (3%). The most common adverse reactions (those occurring in ≥3% of members) in the Doptelet-treated groups (60 mg or 40 mg) across the pooled data from the two trials include pyrexia, abdominal pain, nausea, headache, fatigue, and peripheral edema. For the Low Baseline Platelet Count Cohort, the incidence of serious adverse reactions was 7% (11/159) in the 60 mg Doptelet treatment group and 13% (12/91) in the matching placebo treatment group. For the High Baseline Platelet Count Cohort, the incidence of serious adverse reactions was 8% (9/115) in the 40 mg Doptelet treatment group and 3% (2/65) in the matching placebo treatment group. The most common serious adverse reaction reported with Doptelet was hyponatremia. Two Doptelet-treated members (0.7%) developed hyponatremia as compared to no members in the combined placebo group. Adverse reactions resulting in discontinuation of Doptelet were anemia, pyrexia, and myalgia; each was reported in a single (0.4%) member in the Doptelet (60 mg) treatment group. The efficacy of DOPTELET in adult members with chronic immune thrombocytopenia was

evaluated in a Phase 3, multicenter, randomized, double- blind, placebo- controlled trial (NCT01438840). Members had previously received one or more prior chronic immune thrombocytopenia therapies and had an average of screening and baseline platelet counts <30 x109 /L. Members were centrally stratified by splenectomy status, baseline platelet count (≤15 x109 /L or >15 x109/L to <30 x109/L), and use of concomitant chronic immune thrombocytopenia medication, and then randomized (2:1) to receive either DOPTELET or placebo for 6 months. Members received a starting dose of 20 mg once daily, with doses subsequently titrated based on platelet response. Forty-nine members were randomized, 32 to DOPTELET and 17 to placebo, with similar mean [SD] baseline platelet counts in the 2 treatment groups (14.1 [8.6] x109/L and 12.7 [7.8] x109/L, respectively). The median age was 44 years, 63% were female, and 94% were Caucasian, 4% Asian and 2% Black. The median duration of exposure was 26 weeks for DOPTELET-treated members and 6 weeks for placebo- treated members.

The major efficacy outcome in this trial was the cumulative number of weeks in which the platelet count was ≥50 x109/L during the 6-month treatment period in the absence of rescue therapy. DOPTELET-treated members had a longer duration of platelet counts ≥50 x109 /Lin the absence of rescue therapy than those who received placebo (median 12.4 [0, 25] vs 0 [0, 2] weeks, respectively, p<0.0001).

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Doptelet (avatrombopag) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Doptelet (avatrombopag) include: No labeled contraindications.

Exclusions/Discontinuation:

Discontinue Doptelet if the platelet count does not increase to greater than or equal to 50×109 /L after 4 weeks of dosing at the maximum dose of 40 mg once daily or the maximum dose of 20 mg once daily of the sprinkles.

Discontinue Doptelet if the platelet count is greater than 400×109 /L after 2 weeks of dosing at 20 mg once weekly or 10 mg once weekly of the sprinkles.

OTHER SPECIAL CONSIDERATIONS:

Doptelet should be initiated 10 to 13 days prior to the scheduled procedure. Members should undergo procedure 5 to 8 days after the last dose of Doptelet. A platelet count should be obtained prior to therapy administration and on the day of the procedure.

There is a potential for increased thrombotic risk when administering Doptelet to members with known risk factors for thromboembolism, including genetic prothrombotic conditions (Factor V Leiden, Prothrombin 20210A, Antithrombin deficiency or Protein C or S deficiency).

Doptelet tablets and Doptelet Sprinkle are not substitutable on a mg-to-mg basis. The mixture prepared from the granules in Doptelet Sprinkle capsules is more bioavailable than Doptelet tablets. There is no experience from clinical trials in switching between dosing with the granules and the tablet. If the formulation is switched, monitor platelet counts weekly until stable platelet counts are obtained and adjust dosing as needed before resuming monthly monitoring.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-*

standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.

HCPCS CODE	DESCRIPTION
N/A	

AVAILABLE DOSAGE FORMS:
Doptelet TABS 20MG
Doptelet Sprinkle CPSP 10MG

REFERENCES

1. Doptelet (avatrombopag) tablets, for oral use [prescribing information]. AkaRx, Inc., Durham, NC. July 2025.
2. Terrault N, Chen YC, Izumi N, et al. Avatrombopag Before Procedures Reduces Need for Platelet Transfusion in Members With Chronic Liver Disease and Thrombocytopenia. Gastroenterology 2018; 155:705.
3. Terrault NA, Hassanein T, Howell CD, et al. Phase II study of avatrombopag in thrombocytopenic members with cirrhosis undergoing an elective procedure. J Hepatol 2014;61:1253.
4. Zheng, X. L., Vesely, S. K., Cataland, S. R., Coppo, P., Geldziler, B., Iorio, A., … Peyvandi, F. (2020). ISTH guidelines for treatment of thrombotic thrombocytopenic purpura. Journal of Thrombosis and Haemostasis, 18(10), 2496–2502. doi:10.1111/jth.15010
5. O'Shea, R.S., Davitkov, P., Ko, C.W., Rajasekhar, A., Su, G.L., Sultan, S , … Falck-Ytter, Y. (2021) AGA clinical practice guideline on the management of coagulation disorders in patients with cirrhosis. Gastroenterology, 161(5). Doi: 10.1053/j/gastro.2021.08.015
6. Neunert, C., Terrell, D. R., Arnold, D. M., Buchanan, G., Cines, D. B., Cooper, N., … Vesely, S. K. (2019). American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Advances, 3(23), 3829–3866. https://doi.org/10.1182/bloodadvances.2019000966
7. Northup, P. G., Garcia-Pagan, J. C., Garcia-Tsao, G., Intagliata, N. M., Superina, R. A., Roberts, L. N., … Valla, D. C. (2021). Vascular Liver Disorders, Portal Vein Thrombosis, and Procedural Bleeding in Patients With Liver Disease: 2020 Practice Guidance by the American Association for the Study of Liver Diseases. Hepatology, 73(1), 366–413. https://doi.org/10.1002/hep.31646

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Age Restrictions Quantity FDA-Approved Uses Exclusions/Discontinuation Other Special Considerations	Q4 2025
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Contraindications/Exclusions/Discontinuation Other Special Considerations	Q3 2025

REVISION- Notable revisions: Required Medical Information Duration of Approval Prescriber Requirements References	Q3 2024
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy FDA-Approved Uses Appendix Contraindications/Exclusions/Discontinuation Other Special Considerations Available Dosage Forms References	Q3 2023
REVISION- Notable revisions: Required Medical Information Continuation of Therapy References	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file