

avatrombopag (Doptelet[®], Doptelet Sprinkle)

Policy # 00648

Original Effective Date: 11/21/2018

Current Effective Date: 12/01/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: lusutrombopag (Mulpleta[®]) is addressed separately in medical policy 00650.

Note: eltrombopag Products (Promacta[®], generics, Alvaiz[™]) are addressed separately in medical policy 00627.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member’s contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider avatrombopag (Doptelet[®], Doptelet Sprinkle)[‡] for the treatment of thrombocytopenia to be **eligible for coverage**.^{**}

Patient Selection Criteria

Coverage eligibility for avatrombopag (Doptelet, Doptelet Sprinkle) will be considered when the following criteria are met:

- For **Doptelet** requests:
 - Patient has a diagnosis of chronic liver disease and ALL of the following:
 - Patient is 18 years of age or older; AND
 - Patient has a platelet count less than 50,000 cells per microliter (μL); AND
 - Patient is scheduled to undergo a surgical procedure; OR
 - Patient has a diagnosis of chronic immune thrombocytopenia (ITP) and BOTH of the following:
 - Patient is 6 year of age or older; AND
 - Patient has tried and failed (e.g. intolerance or inadequate response) at least ONE of the following alternative therapies: corticosteroids (e.g., dexamethasone, prednisone), intravenous immunoglobulin (IVIG), anti-D immunoglobulin, a thrombopoietin receptor agonist (e.g., eltrombopag [Promacta[®]][‡], romiplostim [Nplate[®]][‡]), fostamatinib (Tavalisse[™])[‡], or rituximab (Rituxan[®])[‡]; OR
 - Patient has a diagnosis of persistent ITP and BOTH of the following:
 - Patient is 6 years to less than 18 years of age; AND

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- Patient has tried and failed (e.g. intolerance or inadequate response) at least ONE of the following alternative therapies: corticosteroids (e.g., dexamethasone, prednisone), intravenous immunoglobulin (IVIG), anti-D immunoglobulin, a thrombopoietin receptor agonist (e.g., eltrombopag [Promacta], romiplostim [Nplate]), fostamatinib (Tavalisse), or rituximab (Rituxan)
- For **Doptelet Sprinkle** requests:
 - Patient is 1 year to less than 6 years of age; AND
 - Patient has a diagnosis of persistent or chronic immune thrombocytopenia; AND
 - Patient has tried and failed (e.g. intolerance or inadequate response) at least ONE of the following alternative therapies: corticosteroids (e.g., dexamethasone, prednisone), intravenous immunoglobulin (IVIG), anti-D immunoglobulin, a thrombopoietin receptor agonist (e.g., eltrombopag [Promacta], romiplostim [Nplate]), or rituximab (Rituxan).

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of avatrombopag (Doptelet, Doptelet Sprinkle) when patient selection criteria are not met to be **investigational**.*

Background/Overview

Doptelet is an oral thrombopoietin receptor agonist (TPO-RA) that is indicated for treatment of thrombocytopenia in adult patients with chronic liver disease (CLD) who are scheduled to undergo a procedure, in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment, and in pediatric patients 1 year and older with persistent or chronic immune thrombocytopenia who have had an insufficient response to a previous treatment. For patients with CLD scheduled to undergo a procedure, Doptelet should be dosed daily for 5 days beginning 10 to 13 days before the scheduled procedure. The specific daily dose varies based on the patient's baseline platelet count with a higher dose (60 milligrams [mg]) for patients with a platelet count less than 40,000 cells/ μ L and a lower dose (40 mg) for patients with a platelet count between 40,000-50,000 cells/ μ L. For the treatment of chronic ITP in adult and pediatric patients 6 year of age and older, Doptelet should be dosed daily with a starting dose of 20 mg (1 tablet) with dose adjustments to maintain a platelet count of $\geq 50 \times 10^9/L$. In both indications, Doptelet tablets should be given with food. Additionally, Doptelet Sprinkle, a newly available dosage form, is indicated only for pediatric patients aged 1 to less than 6 years with persistent or chronic immune thrombocytopenia who have had an insufficient response to a previous treatment. Doptelet Sprinkle should also be administered with food, and Sprinkle and tablet formulations are not substitutable on a milligram-to-milligram basis.

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Thrombocytopenia is a common, multifactorial phenomenon that affects up to 80% of patients with chronic liver disease. An exact platelet count threshold at which thrombocytopenia is defined is not universal and is dependent upon the individual patient and clinical circumstance. In general, thrombocytopenia is defined as a decrease in the platelet count below the lower limit of normal ($< 150,000/\mu\text{L}$) with subdefinitions based on platelet threshold (e.g., $50,000\text{--}100,000/\mu\text{L}$ is moderate and $< 50,000/\mu\text{L}$ is severe). Thrombocytopenia can adversely affect the management of patients with chronic liver disease and delay necessary diagnostic or surgical procedures due to an increased risk of bleeding. Patients with chronic liver disease and severe thrombocytopenia may receive platelet transfusions prior to surgical procedures to reduce the risk of bleeding. However, the need for platelet transfusions often increases the complexity of the management of the patient due to the possibility for transfusion reactions or the development of antiplatelet antibodies. Promacta and Nplate are two other TPO-RAs with a small amount of off-label data regarding use in this manner, but some safety concerns (e.g. portal vein thrombosis) were noted with these agents.

ITP is an acquired condition of thrombocytopenia in which autoantibodies destroy the platelets and also affect megakaryocytes and impair platelet production. ITP has previously been called idiopathic thrombocytopenic purpura, immune thrombocytopenic purpura, or autoimmune thrombocytopenic purpura, but these terms have been replaced by ITP to reflect the known immunologic mechanism and absence of purpura in some patients. The condition is further classified into newly diagnosed, persistent, or chronic disease based on the time elapsed since diagnosis. ITP is considered persistent when it has been 3-12 months since diagnosis and chronic if it has been more than 12 months. The 2019 American Society of Hematology (ASH) guidelines state that first-line treatment for adults with ITP includes corticosteroids. For patients who are corticosteroid-dependent or do not respond to corticosteroids, thrombopoietin receptor agonists or splenectomy are recommended. Of note, these guidelines only recommend treatment for newly-diagnosed adults with a platelet count $< 30 \times 10^9/\text{L}$ and recommend observation in asymptomatic patients with a platelet count $\geq 30 \times 10^9/\text{L}$.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Doptelet was approved in May 2018 for the treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure. In June 2019, it received the additional indication for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia who have had an insufficient response to a previous treatment. In July 2025, Doptelet received an expanded approval for Doptelet for the treatment of thrombocytopenia in pediatric patients 1 year and older with persistent or chronic ITP who have had an insufficient response to a previous treatment. The expanded approval also included a new dosage form, Doptelet Sprinkle, for use in children 1 to < 6 years of age.

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Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Doptelet for the treatment of thrombocytopenia in patients 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 and ADAPT-2). In each study, patients were assigned to a low baseline platelet count cohort ($< 40 \times 10^9/L$) or a high baseline platelet count cohort (≥ 40 to $< 50 \times 10^9/L$) based on their platelet count at baseline. Patients were then randomized in a 2:1 ratio to either Doptelet or placebo. Patients undergoing neurosurgical interventions, thoracotomy, laparotomy or organ resection were not eligible for enrollment.

In ADAPT-1, a total of 231 patients were randomized, 149 patients were treated with Doptelet and 82 with placebo. In ADAPT-2, a total of 204 patients were randomized, 128 patients were treated with Doptelet and 76 with placebo. Patients underwent a broad spectrum of types of scheduled procedures that ranged from low to high bleeding risk, but the majority of patients (60.8%) underwent low bleeding risk procedures. Among patients, 17.2% underwent procedures with moderate bleeding risk, while 22.1% underwent procedures with high bleeding risk. The major efficacy outcome in both trials was the proportion of patients who did not require a platelet transfusion or any rescue procedure for bleeding after randomization and up to 7 days following an elective procedure. In both baseline platelet count cohorts, patients in the Doptelet treatment groups had a greater proportion of responders than the corresponding placebo treatment groups that were both clinically meaningful and statistically significant. In the low baseline platelet count cohort, 66% of patients in ADAPT-1 and 69% of patients in ADAPT-2 were responders compared with 23% and 35% of the respective placebo groups. In the high baseline platelet count cohort, 88% of patients in both the ADAPT-1 and ADAPT-2 trials were responders compared with 38% and 33% in the respective placebo groups.

The efficacy of Doptelet in adult patients with chronic immune thrombocytopenia (ITP) was evaluated in a phase 3, multicenter, randomized, double-blind, placebo-controlled trial in 49 patients who had previously received at least one prior chronic ITP therapy. Patients were randomized 2:1 to receive either Doptelet or placebo for 6 months. Patients received a starting dose of 20 mg once daily, with doses subsequently titrated based on platelet response. The major efficacy outcome in this trial was the cumulative number of weeks in which the platelet count was greater than or equal to $50 \times 10^9/L$ during the 6-month treatment period in the absence of rescue therapy. Doptelet-treated patients had a longer duration of platelet counts $\geq 50 \times 10^9/L$ than those who received placebo (median 12.4 [0,25] vs 0 [0,2] weeks, respectively, $p < 0.0001$).

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The efficacy and safety of Doptelet was evaluated in pediatric patients ≥ 1 to < 18 years of age with persistent or chronic immune thrombocytopenia in a randomized, double-blind, placebo-controlled trial which included a 12-week randomized treatment phase. Patients were required to have had a diagnosis of primary ITP for ≥ 6 months and had an insufficient response to at least one previous treatment, with an average of 2 baseline platelet counts less than $30 \times 10^9/L$. Patients were randomized (3:1) to receive Doptelet or placebo. The starting dose for patients 6 years and older was 20 mg (tablet), while the starting dose for the youngest cohort was 10 mg (oral granules mixed with a soft food or liquid). Doses could be subsequently titrated based on platelet response. The efficacy of Doptelet in this trial was evaluated by durable platelet response, defined as the proportion of patients achieving at least 6 out of 8 weekly platelet counts $\geq 50 \times 10^9/L$ during the last 8 weeks of the 12-week Treatment Period in the Core Phase in the absence of rescue medication. Efficacy was also evaluated by platelet response, defined as the proportion of subjects achieving at least 2 consecutive platelet assessments $\geq 50 \times 10^9/L$ in the Core Phase in the absence of rescue medication. A durable platelet response was achieved in 27.8% of patients receiving Doptelet versus 0% with placebo (difference of proportion: 27.8%, 95% CI: 15.8–39.7; $p = 0.0077$). Additionally, overall platelet response occurred in 81.5% of Doptelet-treated patients compared to 0% in the placebo group (difference of proportion: 81.5%, 95% CI: 71.1–91.8; $p < 0.0001$).

References

1. Doptelet [package insert]. AkaRx, Inc. Durham, NC. Updated July 2025.
2. Doptelet Drug Evaluation. Express Scripts. Updated May 2018.
3. Neunert C, Terrell DR, Arnold DM, et al. The American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood*. 2019;3(23):3829-3866.

Policy History

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11/08/2018	Medical Policy Committee review
11/21/2018	Medical Policy Implementation Committee approval. New policy.
09/05/2019	Medical Policy Committee review
09/11/2019	Medical Policy Implementation Committee approval. Added coverage criteria and background information for new indication of Doptelet for chronic immune thrombocytopenia.
09/03/2020	Medical Policy Committee review
09/09/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/02/2021	Medical Policy Committee review
09/08/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/01/2022	Medical Policy Committee review
09/14/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

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09/07/2023	Medical Policy Committee review
09/13/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/05/2024	Medical Policy Committee review
09/11/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/06/2025	Medical Policy Committee review
11/12/2025	Medical Policy Implementation Committee approval. Updated title of policy from “avatrombopag (Doptelet)” to “avatrombopag (Doptelet, Doptelet Sprinkle)” to reflect availability of Doptelet sprinkle, which is indicated for pediatric patients aged 1 to less than 6 years with persistent or chronic immune thrombocytopenia who have had an insufficient response to a previous treatment. Added coverage criteria for Doptelet Sprinkle and updated relevant sections.

Next Scheduled Review Date: 11/2026

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 - 1. Consultation with technology evaluation center(s);
 - 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 - 3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and

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- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.