



# Louisiana

## lusutrombopag (Mulpleta<sup>®</sup>)

Policy # 00650

Original Effective Date: 11/21/2018

Current Effective Date: 11/21/2018

*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: avatrombopag (Doptelet<sup>®</sup>) is addressed separately in medical policy 00648.*

### 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 lusutrombopag (Mulpleta<sup>®</sup>)<sup>†</sup> for the treatment of thrombocytopenia to be **eligible for coverage**.<sup>\*\*</sup>

### Patient Selection Criteria

Coverage eligibility for lusutrombopag (Mulpleta) will be considered when the following criteria are met:

- Patient is 18 years of age or older; AND
- Patient has a diagnosis of chronic liver disease; AND
- Patient has a platelet count less than 50,000 cells per microliter ( $\mu\text{L}$ ); AND
- Patient is scheduled to undergo a surgical procedure.

### 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 lusutrombopag (Mulpleta) when patient selection criteria are not met to be **investigational**.\*

### Background/Overview

Mulpleta is an oral thrombopoietin receptor agonist (TPO-RA) that is indicated for treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure. It should be dosed at 3 milligrams (mg) daily for 7 days beginning 8 to 14 days before the scheduled procedure. Mulpleta may be taken with or without food.

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., 50,000-100,000/ $\mu\text{L}$  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

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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.

## **FDA or Other Governmental Regulatory Approval**

### **U.S. Food and Drug Administration (FDA)**

Mulpleta was approved in August 2018 for the treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure.

## **Rationale/Source**

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Mulpleta was evaluated in 2 randomized, double-blind, placebo controlled trials (L-PLUS 1 and L-PLUS 2). Patients with chronic liver disease who were undergoing an invasive procedure and had a platelet count less than  $50 \times 10^9/L$  were eligible to participate. Patients undergoing laparotomy, thoracotomy, open-heart surgery, craniotomy, or organ resection were excluded. In addition, patients with a history of splenectomy, partial splenic embolization, or thrombosis and those with Child-Pugh class C liver disease, absence of hepatopetal blood flow, or a prothrombotic condition other than chronic liver disease were not allowed to participate. In both studies, patients were randomized 1:1 to receive 3 mg of Mulpleta or placebo once daily for up to 7 days. In L-PLUS 1, 57% of patients underwent procedures other than liver ablation/coagulation and in L-PLUS 2, 98% of patients underwent procedures other than liver ablation/coagulation. These other procedures included liver-related procedures (e.g. transcatheter arterial chemoembolization, liver biopsy), upper and lower gastrointestinal endoscopy-related procedures, and procedures such as dental extraction, diagnostic paracentesis, or septoplasty.

In L-PLUS 1, the major efficacy outcome was the proportion of patients who required no platelet transfusion prior to the primary invasive procedure (i.e. a platelet count of  $\geq 50 \times 10^9/L$  with an increase of  $\geq 20 \times 10^9/L$  from baseline). 78% of the 49 Mulpleta patients met this endpoint compared to 13% of the placebo patients. This result was statistically significant.

In L-PLUS 2, the major efficacy outcome was the proportion of patients who required no platelet transfusion prior to the primary invasive procedure and no rescue therapy for bleeding from randomization through 7 days after the primary invasive procedure. 65% of the 108 patients in the Mulpleta group met this endpoint compared to 29% of the 107 patients in the placebo group. This result was statistically significant.

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## References

1. Mulpleta [package insert]. Shionogi, Inc. Boothwyn, PA. Updated August 2018
2. Doptelet Drug Evaluation. Express Scripts. Updated May 2018
3. Mulpleta Drug Evaluation. Express Scripts. Updated September 2018.

## Policy History

Original Effective Date: 11/21/2018

Current Effective Date: 11/21/2018

11/08/2018 Medical Policy Committee review

11/21/2018 Medical Policy Implementation Committee approval. New policy.

Next Scheduled Review Date: 11/2019

\*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 the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated 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
- 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.

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**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.

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