09-J3000-11

Original Effective Date: 12/15/18

Reviewed: 11/09/22

Revised: 12/15/22

Subject: Lusutrombopag (Mulpleta®) Tablet

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Lusutrombopag (Mulpleta®) is an oral small molecule thrombopoietin (TPO) receptor agonist that increases platelet production by stimulating differentiation of megakaryocytes from bone marrow progenitor cells. In July 2018, the US Food and Drug Administration (FDA) approved lusutrombopag for the treatment of thrombocytopenia in adults with chronic liver disease (CLD) who are scheduled to undergo a procedure.

The clinical safety and efficacy of lusutrombopag was evaluated in two double-blind, placebo controlled studies in patients with CLD. Subjects with a platelet count of less than 50 $x10^9$L scheduled to undergo an invasive procedure were included. Individuals scheduled for thoracotomy, laparotomy, open-heart surgery, craniotomy or organ resection were excluded. In addition, those with a history of splenectomy, partial splenic embolization, or thrombosis, Child-Pugh class C liver disease, absence of hepatopetal blood flow, or a prothrombotic condition other than chronic liver disease were also excluded. Subjects underwent various procedures and examples included liver ablation/coagulation (RFA/MCT), transcatheter arterial chemoembolization, liver biopsy, endoscopic variceal ligation, endoscopic injection sclerotherapy, dental extraction, diagnostic paracentesis, removal of cervical polyp, and inguinal hernia repair. Subjects were randomized 1:1 to receive lusutrombopag or placebo for up to 7 days and were scheduled to undergo a procedure 2 to 8 days after the last dose of treatment. The main efficacy outcome in the first trial was the proportion of patients who did not require a platelet transfusion prior to the primary invasive procedure. The main efficacy outcome in the second trial was the proportion of patients who did not require a platelet transfusion prior to the procedure or any rescue therapy for bleeding from randomization and up to 7 days following the procedure. Responders were defined as those who had a platelet count of greater than or equal to 50 $x10^9$L with an increase of greater than or equal to 20 $x10^9$L from baseline.

In trial 1, there were 78% (38/49) of patients who did not require a platelet transfusion prior to the procedure as compared to 13% (6/48) in the placebo group ($p < 0.0001$). In trial 2, there were 65% (70/108) of patients who did not require a platelet transfusion or rescue therapy from bleeding as compared to 29% (31/107) in the placebo group ($p = 0.0001$). In both trials, there was a higher percentage of responders receiving lusutrombopag who achieved a target platelet count of greater than or equal to 50 $x10^9$L as compared to placebo. The most common adverse reaction in patients receiving lusutrombopag was headache.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

I. Initiation of lusutrombopag (Mulpleta®) **meets the definition of medical necessity** when used to treat thrombocytopenia associated with the following conditions:

   A. Chronic liver disease (CLD) and **ALL** of the following are met:

      1. The member's platelet count is less than 50 $x10^9$L
      2. The member is scheduled to undergo an elective procedure with an associated risk of bleeding that would require a platelet transfusion
      3. The elective procedure is scheduled to occur 8 to 14 days after initiation of therapy with lusutrombopag
      4. The member dose not have a history of thrombosis or a genetic prothrombotic condition (e.g., Factor V Leiden, Prothrombin 20210A, Antithrombin deficiency, or Protein C or S deficiency)
      5. The member had an inadequate response or intolerance to avatrombopag (Doptelet)†
      6. Lusutrombopag is not used concurrently with another thrombopoietin receptor agonist (e.g., avatrombopag [Doptelet®], romiplostim [Nplate™], eltrombopag [Promacta])
      7. The dosage does not exceed 3 mg once daily for 7 days

Approval duration: 60 days

†Step therapy requirement does not apply if a prior health plan paid for the medication - documentation of a paid claim within the past 90 days must be submitted

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND

OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Thrombocytopenia in adult patients with chronic liver disease scheduled to undergo a procedure should begin dosing 8 to 14 days prior to a scheduled procedure. Patients should undergo the procedure within 2 to 8 days after the last dose. Take 3 mg with or without food once daily for 7 consecutive days prior to a scheduled procedure. Obtain platelet count prior to administration and not more than 2 days before the scheduled procedure to ensure adequate platelet response.

Drug Availability

- 3 mg tablets

PRECAUTIONS:

Contraindications

- None

Precautions/Warnings

- Thrombotic and thromboembolic complications in patients with chronic liver disease have been associated with thrombopoietin receptor agonists. Consider thrombotic risk when administering to patients with known risk factors for thromboembolism including genetic prothrombotic conditions (Factor V Leiden, Prothrombin 20210A, Antithrombin deficiency, or Protein C or S deficiency). Monitor platelet counts and for thromboembolic events. In patients with ongoing or prior thrombosis or absence of hepatopetal blood flow, only use if the potential benefit justifies the potential risk.
- Do not administer to patients with chronic liver disease to normalize platelet counts.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J8499	Prescription drug, oral, non-chemotherapeutic, Not Otherwise Specified

ICD-10 Diagnoses Codes That Support Medical Necessity

B18.0 – B18.9	Chronic viral hepatitis
C22.0	Hepatocellular carcinoma
K70.0 – K70.9	Alcoholic liver disease
K73.0 – K73.9	Chronic hepatitis, not elsewhere classified
K74.0 – K74.69	Fibrosis and cirrhosis of liver
K75.81	Nonalcoholic steatohepatitis
K76.9	Chronic nonalcoholic liver disease

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: BCBSF has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage:

No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

Eltrombopag (Promacta®), 09-J1000-13
Immune Globulin Therapy, 09-J0000-06
Romiplostim Injection (Nplate™), 09-J0000-88
Avatrombopag (Doptelet), 09-J3000-02

OTHER:

None

REFERENCES:

1. Clinical Pharmacology. [database online]. Tampa, FL: Gold Standard, Inc.; 2022. URL. www.Clinicalpharamcology-ip.com Accessed 10/27/22
2. Micromedex ® Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 10/27/22.
3. Mulpleta (lusutrombopag) [package insert]. Shionogi, Inc. Florham Park, NJ: April 2020.
4. Tateishi R, Seike M, Kudo M et al. A randomized controlled trial of lusutrombopag in Japanese patients with chronic liver disease undergoing radiofrequency ablation. J Gastroenterol. 2018 Aug 13. Doi: 10.1007/s00535-018-1499-2

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the BCBSF Pharmacy Policy Committee on 11/09/22.

GUIDELINE UPDATE INFORMATION:

12/15/18	New Medical Coverage Guideline.
10/15/19	Review and revision to guideline consisting of updating the position statement and references.

01/01/20	Revision to guideline consisting of updating the position statement.
12/15/20	Review and revision to guideline consisting of updating the references.
12/15/21	Review and revision to guideline consisting of updating the references.
12/15/22	Review and revision to guideline; consisting of updating the references.