Original Effective Date: 05/01/2019
Current Effective Date: 09/15/2024
Last P&T Approval/Version: 7/31/2024
Next Review Due By: 07/2025
Policy Number: C16446-A

Mulpleta (lusutrombopag)

PRODUCTS AFFECTED

Mulpleta (lusutrombopag)

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

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.

A. THROMBOCYTOPENIA (WITH CHRONIC LIVER DISEASE):
1. Documented diagnosis of chronic liver disease-associated thrombocytopenia
   AND
2. Prescriber attests the member is scheduled to undergo a procedure (excluding members undergoing laparotomy, thoracotomy, open-heart surgery, craniotomy, or organ resection)
   AND

3. Prescriber attests or the clinical reviewer has found the medication is being initiated 8 to 14 days prior to the scheduled procedure AND the member is undergoing the procedure 2 to 8 days after the last dose
   AND
4. Prescriber attests that a platelet count will be obtained prior to therapy administration and not more than 2 days before the procedure
   AND
5. Documentation the member has a baseline platelet count <50 x10^9/L [DOCUMENTATION REQUIRED]
   AND
6. Prescriber attests or the clinical review has found the medication is NOT being used to normalize platelet counts
   AND
7. Prescriber attests the medication is NOT being used concurrently with another thrombopoietic agent or Spleen Tyrosine Kinase Inhibitor [e.g., Promacta (eltrombopag), Nplate (romiplostim), Doptelet (avatrombopag), or Tavalisse (fostamatinib)]
   AND
8. 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 alternatives for the given diagnosis. Submit documentation including medication(s) tried, dates of trial(s) and reason for treatment failure(s).

CONTINUATION OF THERAPY:
N/A

DURATION OF APPROVAL:
Initial authorization: 7 days, Continuation of therapy: N/A

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a hematologist, hepatologist or surgeon. [If prescribed in consultation, consultation notes must be submitted with initial request.]

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
3 mg once daily for 7 days

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

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Mulpleta is a small molecule thrombopoietin (TPO) receptor agonist that interacts with the transmembrane domain of human TPO receptors expressed on megakaryocytes to induce the proliferation and differentiation of megakaryocytic progenitor cells from hematopoietic stem cells and megakaryocyte maturation. It is administered orally as a tablet and is indicated for the treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure.
Efficacy
The efficacy of Mulpleta for the treatment of thrombocytopenia in patients with chronic liver disease who are scheduled to undergo a procedure was evaluated in 2 randomized, double-blind, placebo-controlled trials (L-PLUS 1 (N=97) and L-PLUS 2 (N=215; NCT02389621)). Patients with chronic liver disease who were undergoing an invasive procedure and had a platelet count less than 50 × 10/L were eligible to participate. Patients undergoing laparotomy, thoracotomy, open-heart surgery, craniotomy, or organ resection were excluded. Patients with a history of splenectomy, partial splenic embolization, or thrombosis and those with Child-Pugh class C liver disease, absence of hepatoportal blood flow, or a prothrombotic condition other than chronic liver disease were not allowed to participate. The member populations were similar between the Mulpleta and placebo arms and consisted of 60% male and 40% female; median age was 60 years (range 19-88). The racial and ethnic distribution was White (55%), Asian (41%), and Other (4%). Patients were randomized 1:1 to receive 3 mg of Mulpleta or placebo once daily for up to 7 days. Randomization was stratified by liver ablation/coagulation or other procedures and the platelet count at screening/baseline. In L- PLUS 1, 57% of patients underwent procedures other than liver ablation/coagulation and 43% underwent liver ablation/coagulation (RFA/MCT). In L-PLUS 2, 98% of patients underwent procedures other than liver ablation/coagulation and 2% underwent liver ablation/coagulation (RFA/MCT). Procedures other than liver ablation/coagulation (RFA/MCT) included liver-related procedures (transcatheter arterial chemoembolization, liver biopsy, and others), upper and lower gastrointestinal endoscopy-related procedures (endoscopic variceal ligation, endoscopic injection sclerotherapy, polypectomy, and biopsy), and other procedures (dental extraction, diagnostic paracentesis or laparocentesis, septoplasty, embolization of splenic artery aneurysm, bone marrow biopsy, removal of cervical polyp, and inguinal hernia repair (non- laparotomy based)). In L-PLUS 1, the major efficacy outcome was the proportion of patients who require no platelet transfusion prior to the primary invasive procedure. In L-PLUS 2, the major efficacy outcome was the proportion of patients who require no platelet transfusion prior to the primary invasive procedure and no rescue therapy for bleeding (i.e., platelet preparations, other blood preparations, including red blood cells and plasma, volume expanders) from randomization through 7 days after the primary invasive procedure. In both trials, additional efficacy outcomes included the proportion of patients who require no platelet transfusion during the study, proportion of responders, duration of the increase in platelet count defined as the number of days during which the platelet count was maintained as ≥50 × 10 /L, and the time course of platelet counts. In both the L-PLUS 1 and L-PLUS 2 trials, responders were defined as patients who had a platelet count of≥50 × 10 /L with an increase of ≥20 × 10 /L from baseline. In the L-PLUS 1 trial, the proportion of patients not requiring platelet transfusion prior to invasive procedure was 78% (38/49) and the proportion of responders was 76% (37/49). In the L- PLUS 2 trial, the proportion of patients not requiring platelet transfusion prior to invasive

procedure or rescue therapy for bleeding through7 days after invasive procedure was 65% (70/108) and the proportion of responders was 65% (70/108).

Safety

The safety of Mulpleta was evaluated in 3 randomized, double-blind, placebo-controlled trials, LPLUS 1, L-PLUS 2, and M0626, in which patients with chronic liver disease and thrombocytopenia were treated with Mulpleta (N=171) or placebo (N=170) at a dose of 3 mg daily for up to 7 days prior to a scheduled procedure. The majority of patients were males (59%), and median age was 61 years (range 19-88). The racial and ethnic distribution was White (50%), Asian (47%), Black (<1%), and Other (3%). The most common adverse reaction in the Mulpleta treated group across the pooled data from the three trials was headache (5%). The incidence of serious adverse events was 5% (9 of 171 patients) in the Mulpleta group and 7% (12 of 170 patients) in the placebo group. The most common serious adverse reaction reported with Mulpleta was portal vein thrombosis. No adverse reactions resulted in the discontinuation of Mulpleta.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Mulpleta (lusutrombopag) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Mulpleta (lusutrombopag) include: No labeled contraindications. Mulpleta should not be used to normalize platelet counts.

OTHER SPECIAL CONSIDERATIONS:

Mulpleta should be started 8 to 14 days prior to the scheduled procedure. Patients should undergo procedure 2 to 8 days after the last dose. A platelet count should be obtained prior to therapy administration and not more than 2 days before the procedure.

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

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:

Mulpleta TABS 3MG

REFERENCES

1. Mulpleta (lusutrombopag) tablet [prescribing information]. Shionogi INC., Florham Park, NJ. April 2020.
2. Katsube T, Ishibashi T, Kano T, Wajima T. Population Pharmacokinetic and Pharmacodynamic Modeling of Lusutrombopag, a Newly Developed Oral Thrombopoietin Receptor Agonist, in Healthy Subjects. Clin Pharmacokinet 2016; 55:1423.
3. Kim ES. Lusutrombopag: First Global Approval. Drugs 2016; 76:155.
4. 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
5. 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 Prescriber Requirements References	Q3 2024
REVISION- Notable revisions: Required Medical Information Contraindications/Exclusions/Discontinuation Other Special Considerations Available Dosage Forms References	Q3 2023
REVISION- Notable revisions: Required Medical Information	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file