

PHARMACY POLICY STATEMENT

Marketplace

DRUG NAME	Mulpleta (lusutrombopag)
BENEFIT TYPE	Pharmacy
STATUS	Prior Authorization Required

Mulpleta, approved by the FDA in 2018, is a small molecule thrombopoietin (TPO) receptor agonist indicated for the treatment of thrombocytopenia in adult patients with chronic liver disease (CLD) who are scheduled to undergo a procedure. The agonistic effect upregulates the production of platelets. Mulpleta should not be administered in an attempt to normalize platelet counts. TPO receptor agonists have been associated with thrombotic and thromboembolic complications. Approval of Mulpleta was based on the placebo-controlled L-PLUS 1 and L-PLUS 2 clinical trials. Doptelet is another TPO receptor agonist (TPO-RA) with the same indication as Mulpleta. TPO is important for regulating thrombopoiesis.

Thrombocytopenia is a condition of low platelet counts. It is the most common hematologic complication in patients with CLD, and 1% experience severe thrombocytopenia (platelet count $<50,000/\mu\text{L}$). Advanced disease often requires numerous medical and/or surgical diagnostic and therapeutic procedures. Thrombocytopenia may be associated with increased bleeding risk in these invasive procedures. Mulpleta has been shown to reduce the need for platelet transfusions and achieve a durable platelet response.

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

Thrombocytopenia with chronic liver disease (CLD)

For **initial** authorization:

- Member is at least 18 years of age; AND
- Medication must be prescribed by or in consultation with a hematologist, hepatologist, or gastroenterologist; AND
- Member has a documented diagnosis of chronic liver disease (CLD); AND
- Member has a diagnosis of severe thrombocytopenia with a platelet count $< 50 \times 10^9/\text{L}$ within the last 30 days; AND
- Member is scheduled to undergo an invasive procedure; AND
- Member does NOT have any of the following:
 - History of liver transplantation
 - Congenital, drug-induced, or immune thrombocytopenia; AND
- Mulpleta is not being prescribed with another TPO receptor agonist such as Doptelet.
- Dosage allowed/Quantity limit:** 3 mg once daily for 7 days. Begin 8-14 days prior to procedure; undergo procedure 2-8 days after last dose.
QL: 7 tablets

If all the above requirements are met, the medication will be approved for 1 month.

For **reauthorization**:

- Mulpleta will not be reauthorized for continuous use.

CareSource considers Mulpleta (lusutrombopag) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
07/24/2019	New policy for Mulpleta created.
01/20/2023	Transferred to new template. Updated and added references. Added hepatology and GI as accepted specialists. Specified platelet lab must be within past 30 days. Shortened list of exclusions. Added no concomitant use with another TPO-RA.
08/08/2025	Removed thrombosis exclusion (not an absolute contraindication; must monitor).

References:

1. Mulpleta [prescribing information]. Shionogi Inc.; 2020.
2. Peck-Radosavljevic M, Simon K, Iacobellis A, et al. Lusutrombopag for the Treatment of Thrombocytopenia in Patients With Chronic Liver Disease Undergoing Invasive Procedures (L-PLUS 2). *Hepatology*. 2019;70(4):1336-1348. doi:10.1002/hep.30561
3. Orme ME, Bentley R, Marcella S, et al. Systematic Review with Meta-Analysis: Efficacy and Safety of Lusutrombopag for Severe Thrombocytopenia in Patients with Chronic Liver Disease Undergoing Invasive Procedures. *Adv Ther*. 2022;39(9):4169-4188. doi:10.1007/s12325-022-02235-w
4. Hayashi H, Beppu T, Shirabe K, Maehara Y, Baba H. Management of thrombocytopenia due to liver cirrhosis: a review. *World J Gastroenterol*. 2014;20(10):2595-2605. doi:10.3748/wjg.v20.i10.2595
5. Peck-Radosavljevic M. Thrombocytopenia in chronic liver disease. *Liver Int*. 2017;37(6):778-793. doi:10.1111/liv.13317
6. Lim HJ, Cuker A. Thrombocytopenia and liver disease: pathophysiology and periprocedural management. *Hematology Am Soc Hematol Educ Program*. 2022;2022(1):296-302. doi:10.1182/hematology.2022000408
7. Miller JB, Figueroa EJ, Haug RM, Shah NL. Thrombocytopenia in Chronic Liver Disease and the Role of Thrombopoietin Agonists. *Gastroenterol Hepatol (N Y)*. 2019;15(6):326-332.
8. Flisiak R, Antonov K, Drastich P, et al. Practice Guidelines of the Central European Hepatologic Collaboration (CEHC) on the Use of Thrombopoietin Receptor Agonists in Patients with Chronic Liver Disease Undergoing Invasive Procedures. *J Clin Med*. 2021;10(22):5419. Published 2021 Nov 19. doi:10.3390/jcm10225419

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Revised date: 08/08/2025