Reference number(s)
4856-A

STANDARD MEDICARE PART B MANAGEMENT

CABLIVI (caplacizumab-yhdp)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Cablivi is indicated for the treatment of adult patients with acquired thrombotic thrombocytopenic purpura (aTTP), in combination with plasma exchange and immunosuppressive therapy.

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. DOCUMENTATION

The following documentation must be available, upon request, for all submissions: For continuation of therapy, medical record documentation of signs of persistent underlying aTTP.

III. CRITERIA FOR INITIAL APPROVAL

Acquired thrombotic thrombocytopenic purpura (aTTP)
Authorization of 30 days may be granted for treatment of acquired thrombotic thrombocytopenic purpura (aTTP) after the plasma exchange period in the inpatient setting when all of the following criteria are met:
1. The member received the requested medication with plasma exchange.
2. The requested medication will be given in combination with immunosuppressive therapy.
3. The member will not receive the requested medication beyond 30 days from the cessation of plasma exchange unless the member has documented persistent aTTP.
4. The member has not experienced more than 2 recurrences of aTTP while on the requested medication. (A recurrence is when the member needs to reinitiate plasma exchange. A 28-day extension of therapy does not count as a recurrence.)

IV. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization for 28 days may be granted when all of the following criteria are met:

1. The member is currently receiving therapy with Cablivi
2. Cablivi is being used to treat an indication enumerated in Section III
3. The request for continuation of therapy is for extension of therapy after the initial course of the requested medication (initial course: treatment with the requested medication during and 30 days after plasma exchange).
4. The member has either of the following documented signs of persistent underlying aTTP:
   a. ADAMTS13 activity level less than 10% or
   b. All of the following:
      i. Microangiopathic hemolytic anemia (MAHA) documented by the presence of schistocytes on peripheral smear, and
      ii. Thrombocytopenia (platelet count below normal per laboratory reference range), and
      iii. Elevated lactate dehydrogenase (LDH) level (LDH level above normal per laboratory reference range)
5. The requested medication will be given in combination with immunosuppressive therapy.
6. The member has not received a prior 28-day extension of therapy after the initial course of the requested medication for this course of treatment.
7. The member has not experienced more than 2 recurrences of aTTP while on the requested medication. (A recurrence is when the member needs to reinitiate plasma exchange. A 28-day extension of therapy does not count as a recurrence.)

V. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:

1. The prescribing information for Cablivi.
2. The available compendium
   a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
   b. Micromedex DrugDex
   c. American Hospital Formulary Service- Drug Information (AHFS-DI)
   d. Lexi-Drugs
   e. Clinical Pharmacology
3. Consensus on the standardization of terminology in thrombotic thrombocytopenic purpura and related thrombotic microangiopathies.
4. Guidelines on the diagnosis and management of thrombotic thrombocytopenic purpura and other thrombotic microangiopathies.
5. Rituximab prophylaxis to prevent thrombotic thrombocytopenic purpura relapse: outcome and evaluation of dosing regimens.

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Cablivi are covered.

VI. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for the above continuation of therapy criteria for continued use of Cablivi to treat acquired thrombotic thrombocytopenic purpura can be found in the prescribing information and the phase III trial. If the member is still exhibiting a suppressed ADAMTS13 level after 30 days of initial therapy, the prescribing information

indicates treatment may be extended for a maximum of 28 days. Clinical presentation of TTP includes the presence of both thrombocytopenia and microangiopathic hemolytic anemia with schistocytes seen on blood smear. In the study published by the HERCULES Investigators (Scully 2019), LDH level above the upper limit of normal was used as a secondary endpoint to evaluate the effect of Cablivi for refractory disease. The primary outcome was the time to a response, which was defined as the time from the first intravenous administration of caplacizumab or placebo to normalization of the platelet count (i.e., a platelet count of at least 150,000 per cubic millimeter), with discontinuation of daily plasma exchange within 5 days thereafter. The four key secondary outcomes, which were hierarchically ranked on the basis of clinical relevance, were the following: a composite of TTP-related death, recurrence of TTP, or a major thromboembolic event during the trial treatment period; recurrence of TTP at any time during the trial, including the follow-up period; refractory TTP (defined by the lack of a doubling of the platelet count after 4 days of treatment and a lactate dehydrogenase level that remained above the upper limit of the normal range); and the time to normalization (i.e., to a level below the defined upper limit of the normal range) of three organ-damage markers (lactate dehydrogenase, cardiac troponin I, and serum creatinine). A recurrence was defined as a new decrease in the platelet count that necessitated the reinitiation of plasma exchange after normalization of the platelet count had occurred. An exacerbation was defined as a recurrence that occurred within 30 days after the last plasma exchange. A relapse was defined as a recurrence that occurred more than 30 days after cessation of plasma exchange.

VII. REFERENCES

1. Cablivi [package insert]. Cambridge, MA: Genzyme Corporation; February 2022.
2. Scully M, Cataland SR, Peyvandi F; et al. Caplacizumab treatment for acquired thrombotic thrombocytopenic purpura. *N Engl J Med*. 2019;380(4):335-346.
3. Sadler JE. Pathophysiology of thrombotic thrombocytopenic purpura. *Blood.* 2017;130(10):1181-1188.
4. Scully M, Cataland S, Coppo P, et al. Consensus on the standardization of terminology in thrombotic thrombocytopenic purpura and related thrombotic microangiopathies. *J Thromb Haemost*. 2017; 15(2):312-322.
5. Scully M, Hunt BJ, Benjamin S, et al. Guidelines on the diagnosis and management of thrombotic thrombocytopenic purpura and other thrombotic microangiopathies. *Br J Haematol*. 2012;158(3)323-335.
6. Westwood JP, Thomas M, Alwan F, et al. Rituximab prophylaxis to prevent thrombotic thrombocytopenic purpura relapse: outcome and evaluation of dosing regimens. *Blood Adv.* 2017; 1(15):1159-1166.