Caplacizumab-yhdp (Cablivi®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO012

Description

Caplacizumab-yhdp (Cablivi) is a von Willebrand factor (vWF) - directed antibody fragment (called a Nanobody) that inhibits the interaction between vWF and platelets, thereby reducing both vWF-mediated platelet adhesion and platelet consumption.

Length of Authorization

- Initial: 30 days
- Renewal: 28 days

Quantity limits

Dosage Form	Indication	Quantity Limit	DDID
Initial Request			
11mg vial	aTTP	30 vials/30 days	205773
Renewal Request			
11mg vial	aTTP	28 vials/28 days	205773

Initial Evaluation

I. Caplacizumab-yhdp (Cablivi) may be considered medically necessary when the following criteria below are met:
   A. Member is an adult age 18 and over; **AND**
   B. Prescribed in consultation with a hematologist; **AND**
   C. First administration will be done as an inpatient intravenous bolus infusion under the supervision of a healthcare professional; **AND**
   D. Caplacizumab (Cablivi) will be continued for 30 days beyond the last plasma exchange; **AND**
   E. A diagnosis of **acquired thrombotic thrombocytopenic purpura (aTTP)** when the following are met:
      1. Member has thrombocytopenia and microscopic evidence of red blood cell fragmentation (e.g. schistocytes); **AND**
      2. Taken in a regimen that includes both plasma exchange and an immunosuppressant (i.e. Rituximab, glucocorticoids); **AND**
      3. One of the following:
         i. A suppressed or deficient level of ADAMTS13*
         ii. A PLASMIC score to indicate an intermediate to high risk of ADAMTS13 deficiency, defined as a level less than or equal to 10% (5 to 7 points).
         iii. Presentation of severe features, including, but not limited to the following:

a. Neurologic findings such as seizures, focal weakness, aphasia, dysarthria, confusion, coma
b. Symptoms suggesting encephalopathy
c. High serum troponin levels

II. Caplacizumab (Cablivi) is considered not medically necessary when criteria above are not met and/or when used for:
   A. Adjunct to treatments of thrombocytopenia other than plasma exchange and immunosuppressant.

III. Caplacizumab (Cablivi) is considered investigational when used for all other conditions, including but not limited to:
   A. Idiopathic thrombocytopenia
   B. Hereditary thrombotic thrombocytopenic purpura (TTP)
   C. Drug-induced thrombotic microangiopathy
   D. Hemolytic uremic syndrome
   E. Complement-mediated TMA
   F. Diarrheal hemolytic uremic syndrome
   G. Thrombocytopenia in pregnancy

Renewal Evaluation

I. Member has received caplacizumab (Cablivi) in combination with plasma exchange and immunosuppressive therapy for 30 days beyond the last plasma exchange; **AND**
II. Member has documented signs of persistent underlying disease with documentation of suppressed ADAMTS13 activity level; **AND**
III. Treatment will be extended one-time for a maximum of 28 days following the initially approved treatment course; **AND**
IV. Patient has not experienced more than 2 recurrences* while on caplacizumab (Cablivi).

Supporting Evidence

I. Caplacizumab (Cablivi) was studied and approved for the treatment of aTTP combination with plasma exchange and immunosuppressant in adult subjects age 18 years and older, under the supervision of a medical specialist.
II. Initial administration is performed as an inpatient, by intravenous bolus infusion, followed by subcutaneous injection. There is the potential for outpatient self-administration of subcutaneous injection, especially following the discontinuation of plasma exchange.

III. Diseases of thrombotic microangiopathy have varied etiologies and rule-out of differential diagnoses is important to determine effective and safe therapy. In practice, most hospitals do not have access to on-site testing for ADAMTS13 level. Results are typically delayed by use of off-site laboratories for confirmation as standard therapy is initiated.
- An ADAMTS13 level is of less than ten percent would indicate a severe case;
- Laboratory outcome may be pending at time of initial authorization request;
- Laboratory outcome of ADAMTS13 is required upon renewal request.

IV. The PLASMIC scoring system is a validated diagnostic tool used to discriminate between the likelihood of ADAMSTS13 deficiency and other potential causes of microangiopathic hemolysis.
- Scoring
    i. Low risk category
        1. Score of 0-4
        2. Indicates a risk of severe ADAMTS13 deficiency (levels less than or equal to 10%) in 4.3%.
    ii. Intermediate risk category
        1. Score of 5-6
        2. Indicates a 56.8% likelihood of severe ADAMTS13 deficiency involvement.
    iii. High risk category
        1. Score of 7
        2. Indicates a 96.2% likelihood of severe ADAMTS13 deficiency
- Pre-existing liver or renal disease can falsely lower PLASMIC score.

V. Standard therapy of plasma exchange is initiated as soon as possible to mitigate the progressive course of neurologic deterioration, cardiac ischemia, irreversible renal failure and death.

VI. Treatment of initial acute episode with caplacizumab (Cablivi) is continued for at least 30 days following the last plasma exchange.

VII. *Terminology used in the setting of aTTP include the following:
- Response: normalization or stabilization of platelet count with plasma exchange.
- Remission: maintenance of normal platelet count for 30 days after stopping plasma exchange.
- Relapse: recurrence of TTP following remission.
- Exacerbation: recurrent thrombocytopenia within 30 days of stopping plasma exchange

VIII. The extension of treatment in the event of relapse may be considered when member experiences one of the following:

- A return of the clinical signs and symptoms of aTTP;
- Deficient ADAMTS13 level.

Investigational or Not Medically Necessary Uses

I. Include but are not limited to: Idiopathic thrombocytopenia, hereditary thrombotic thrombocytopenic purpura (TTP), drug-induced thrombotic microangiopathy, hemolytic uremic syndrome, complement-mediated TMA, thrombocytopenia in pregnancy
   A. Diseases of thrombotic microangiopathy have varied etiologies and effective therapies.
   B. Acquired thrombolic thrombocytopenia purpura is due to severely deficient levels of protease ADAMTS13, which manages thrombotic microangiopathy by limiting uncleaved vWF. Uncleaved vWF cause platelet consumption and thrombic microangiopathy by adhesion to platelets.
   C. Caplacizumab (Cablivi) prevents adhesion between vWF and platelets.

References

1. Cablivi [prescribing information]. Cambridge, MA: Genzyme Corporation; February 2019.
2. FDA approves first therapy for the treatment of adult patients with a rare blood clotting disorder. https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm630851.htm
3. UpToDate, Inc. Acquired TTP: Clinical manifestations and diagnosis. UpToDate [Online Database]. Waltham, MA. Last updated April 23, 2018. Available from: http://uptodate.com/home/index.html. Accessed February 12, 2019.
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5. Scully M, Cataland SR, Peyvandi F, et al. Caplacizumab treatment for acquired thrombotic thrombocytopenic purpura. NEJM; Jan 2019; 380(4): 335-46.
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8. Sadler, JE. Pathophysiology of thrombotic thrombocytopenic purpura. Blood; Sept 2017; 130(10): 1181-88..
9. Bendapudi PK, et al. Derivation and external validation of the PLASMIC score for rapid assessment of adults with thrombotic microangiopathies: a cohort study. Lancet Hematology 2017;4:e157-64
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Last Updated	
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Action and Summary of Changes	Date
