09-J3000-32

Original Effective Date: 06/15/19

Reviewed: 02/14/24

Revised: 03/15/24

Subject: Caplacizumab-yhdp (Cablivi®)

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DESCRIPTION:

Acquired or immune-mediated thrombotic thrombocytopenic purpura (aTTP) is a thrombotic microangiopathy caused by deficiency of the von Willebrand factor (vWF) cleaving protein, ADAMTS13, which results in thrombocytopenia, microangiopathic hemolytic anemia, multiorgan dysfunction, thrombosis and death. Diagnosis is based on clinical presentation and severe ADAMTS13 deficiency with levels of less than 10%. Treatment includes daily plasma exchange and immunosuppressive therapy with glucocorticoids.

Caplacizumab-yhdp (Cablivi) was approved by the Food and Drug Administration (FDA) in February 2019 for the treatment of adult patients with acquired TTP (aTTP), in combination with plasma exchange and immunosuppressive therapy. Caplacizumab-yhdp is a vWF-directed antibody fragment that inhibits the interaction between vWF and platelets, which reduces both vWF-mediated platelet adhesion and platelet consumption.

The efficacy of caplacizumab was evaluated in a double-blind, placebo-controlled trial in combination with plasma exchange and immunosuppressive therapy. Patients were included if they had TTP based on clinical presentation (presence of both thrombocytopenia and microangiopathic hemolytic anemia with schistocytes seen on blood smear). Severe ADAMTS13 deficiency was not required for eligibility but was below 10% in 85% of patients at baseline. Patient were excluded if they had suspected thrombotic microangiopathies that were not associated with TTP, such as hemolytic uremic syndrome, or if they had congenital TTP. Patients received a single 11 mg intravenous bolus of caplacizumab (n=72) or placebo (n=73) prior to the first plasma exchange after randomization, followed by daily subcutaneous injection of 11 mg of caplacizumab or placebo until 30 days following the last plasma exchange. If signs of persistent disease remained (such as suppressed ADAMTS13 activity levels), treatment was continued for 7 day intervals to a maximum of 28 days. The median duration of treatment was 35 days. The

primary efficacy endpoint was time to normalization of the platelet count (defined as 150 x 10^9/L), with discontinuation of daily plasma exchange within 5 days thereafter. The caplacizumab treatment group showed a significant improvement in time to platelet count normalization as compared to placebo (2.69 vs 2.88 days for 50th percentile; 2.95 vs 4.5 days for 75th percentile) and were 1.55 times as likely to have a normalization of platelet count (CI 1.09 to 2.19). The secondary outcome of was the composite TTP-related death (0 vs. 4.1%), recurrence of TTP (4.2% vs 38.4%), and major thromboembolic event (8.5 vs 8.2%) which overall occurred in fewer patients in the caplacizumab group as compared to placebo (12% vs 49%, p<0.001). The number of days of plasma exchange, days hospitalized, and days in the intensive care unit were all lower in the caplacizumab treatment group. The most common adverse reactions were epistaxis, gingival bleeding, urticaria, headache, fatigue, pyrexia, dyspnea and injection site hemorrhage. Bleeding events occurred more frequently with caplacizumab treatment as compared to placebo (58% vs 43%).

POSITION STATEMENT:

Initiation of caplacizumab-yhdp (Cablivi) **meets the definition of medical necessity** for the treatment of the following indications when all of the specific criteria are met:

1. Acquired thrombotic thrombocytopenic purpura (aTTP)
    A. **ONE** of the following - documentation must be submitted:
        i. Presence of thrombocytopenia (<100 x 10^9/L) and microscopic evidence of red blood cell fragmentation (e.g., schistocytes on blood smear)
        ii. Severe ADAMTS13 deficiency (<10%)
    B. Member will receive plasma exchange and immunosuppressants (e.g. prednisone, prednisolone) in combination with caplacizumab during the initial treatment period
    C. Member does not have hemolytic uremic syndrome or congenital TTP
    D. Member has not experienced more than 2 recurrences of aTTP while receiving caplacizumab*
    E. The dose does not exceed the following:
        i. 11 mg intravenously on the first day prior to plasma exchange
        ii. 11 mg subcutaneously daily following plasma exchange and up to 30 days following the last plasma exchange

Approval duration: 6 weeks

Continuation of caplacizumab-yhdp (Cablivi) **meets the definition of medical necessity** for the treatment of acquired TTP when **ALL** of the following criteria are met:

1. An authorization or reauthorization has been previously approved by Florida Blue or another health plan in the past 2 months for caplacizumab-yhdp, **OR** the member has previously met **ALL** indication-specific criteria.
2. The member is requesting a one month (28 day) extension of therapy after the initial course of treatment (the initial course includes treatment with plasma exchange and the 30 days following plasma exchange)

3. Member has a continued need for treatment as indicated by **ONE** of the following – documentation must be submitted
    A. Presence of thrombocytopenia (<100 x 10^9/L) and microscopic evidence of red blood cell fragmentation (e.g., schistocytes on blood smear)
    B. Severe ADAMTS13 deficiency (<10%)
4. Member has not experienced more than 2 recurrences of aTTP while receiving caplacizumab*
5. The dose does not exceed 11 mg daily for a maximum of 28 days

Approval duration: 5 weeks

*Note: Recurrence is defined as thrombocytopenia after an initial recovery of the platelet count that requires the need to reinitiate plasma exchange

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

- Caplacizumab-yhdp is indicated for the treatment of adult patients with acquired thrombotic thrombocytopenic purpura (aTTP), in combination with plasma exchange and immunosuppressive therapy. Caplacizumab should be administered upon the initiation of plasma exchange therapy.
- First day of treatment: 11 mg bolus intravenous injection at least 15 minutes prior to plasma exchange followed by an 11 mg subcutaneous injection after completion of plasma exchange on day 1.
- Subsequent treatment during daily plasma exchange: 11 mg subcutaneous injection once daily following plasma exchange.
- Treatment after the plasma exchange period: 11 mg subcutaneous injection once daily for 30 days beyond the last plasma exchange.
- If after initial treatment course, signs of persistent underlying disease such as suppressed ADAMTS13 activity levels remain present, treatment may be extended for a maximum of 28 days.
- Discontinue if the patient experiences more than 2 recurrences of aTTP while on caplacizumab
- The first dose should be administered by a healthcare provider as a bolus intravenous injection. Administer subsequent doses subcutaneously in the abdomen.

Dose Adjustments

- The effect of hepatic impairment is unknown; closely monitor for bleeding in patients with severe hepatic impairment.

Drug Availability

- 11 mg as a lyophilized powder in a single-dose vial

PRECAUTIONS:

Boxed Warning

- none

Contraindications

- Previous severe hypersensitivity reaction to caplacizumab-yhdp or any of the excipients.

Precautions/Warnings

- Bleeding: Severe bleeding can occur; risk is increased in patients with underlying coagulopathies. If clinically significant bleeding occurs, interrupt treatment. Withhold caplacizumab 7 days prior to elective surgery, dental procedures, or other invasive interventions.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

C9047	Injection, caplacizumab-yhdp, 1 mg (hospital outpatient use ONLY)
J3590	Unclassified biologicals

ICD-10 Diagnoses Codes That Support Medical Necessity

M31.10	Thrombotic microangiopathy, unspecified

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: Florida Blue 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:

Thrombocytopenia: a reduced level of circulating platelets, which are cell fragments that normally assist with blood clotting.

RELATED GUIDELINES:

Rituximab (Rituxan), 09-J0000-59

OTHER:

None Applicable

REFERENCES:

1. Cablivi [prescribing information]. Genzyme Corporation. Cambridge, MA. April 2023.
2. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2024 [cited 2024 Feb 1]. Available from: http://www.clinicalpharmacology.com/.
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4. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2024 [cited 2024 Feb 1]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/
5. Peyvandi F, Scully M, Kremer JA et al. Caplacizumab for Acquired thrombotic thrombocytopenic purpura. New Engl J Med. 2016; 374:511-22.
6. Scully M, Cataland SR, Peyvandi F et al. Caplacizumab treatment for acquired thrombotic thrombocytopenic purpura. New Engl J Med. 2019; 380: 335-346.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 02/14/24.

GUIDELINE UPDATE INFORMATION:

06/15/19	New Medical Coverage Guideline.
07/01/19	Revision: Added HCPCS code C9047.
10/15/20	Review and revision to guideline; consisting of update to the position statement and references.
10/01/21	ICD-10 coding update.
12/15/21	Review and revision to guideline; consisting of updating dosing and references.
01/15/21	Review and revision to guideline; consisting of updating the position statement.
03/15/24	Review and revision to guideline; consisting of updating references.