Clinical Policy: Caplacizumab-yhdp (Cablivi)

Reference Number: PA.CP.PHAR.416
Effective Date: 04/2019
Last Review Date: 04/2023

Revision Log

Description
Caplacizumab-yhdp (Cablivi®) is a von Willebrand factor (vWF)-directed antibody fragment.

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

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Cablivi is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Acquired Thrombotic Thrombocytopenic Purpura (must meet all)**:**

1. Diagnosis of aTTP confirmed by one of the following:
   a. with ADAMTS13 activity < 10% of normal;
   b. PLASMIC score of 6 to 7 (*see Appendix D*);
2. Prescribed by or in consultation with a hematologist;
3. Age ≥ 18 years;
4. Prescribed in combination with plasma exchange therapy;
5. Prescribed in combination with immunosuppressive therapy (i.e., glucocorticoids, rituximab);
   **Prior authorization is required for rituximab*
6. Dose does not exceed (a and b) (*see Section V)*:
   a. Loading dose on Day 1: 11mg pre-plasma exchange and 11mg post-plasma exchange (22 mg total);
   b. Maintenance: 11 mg per day.

Approval duration: 30 days

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

II. Continued Therapy

A. Acquired Thrombotic Thrombocytopenic Purpura (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;;
2. Member meets one of the following (a or b):
   a. If request is for a new treatment cycle, both of the following (i or ii):

i. Member has experienced no more than two recurrences (*see Appendix D*) while taking Cabliv;
ii. Cablivi is prescribed in combination with plasma exchange and immunosuppressive therapy (i.e., glucocorticoids, rituximab);

b. If request is for treatment extension, all of the following (i, ii, and iii):
i. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters: increase in platelet counts, reduction in neurological symptoms, or improvements in organ-damage markers (lactate dehydrogenase, cardiac troponin I, and serum creatinine);
ii. Member continues to have signs of persistent underlying disease (e.g., suppressed ADAMTS13 activity levels remain present);
iii. Member has received no more than 58 days of Cablivi therapy after completion of plasma exchange therapy;

3. Dose does not exceed the following (a or b):
a. For new treatment cycle: loading dose of 22 mg on day 1, followed by maintenance dose of 11 mg per day;
b. For treatment extension: 11 mg per day.

Approval duration:
New treatment cycle - 30 days
Treatment extension - up to a total duration of 58 days post plasma-exchange

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – PA.CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

aTTP: acquired thrombotic thrombocytopenic purpura
FDA: Food and Drug Administration
FFP: fresh frozen plasma
PEX: plasma exchange
vWF: von Willebrand factor

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Plasma Exchange (PEX) • Fresh Frozen Plasma (FFP) • Solvent detergent/viral-inactivated plasma • Cryosupernatant	1 to 1.5x estimated plasma volume daily until two days after normalization of platelet count (≥ 150 x 10^9/L).	1 to 1.5x estimated plasma volume
methylprednisone (Solu-Medrol®)	1mg/kg/day IV or PO during PEX and continued for 1 week after PEX. Tapered with the goal of being corticosteroid-free by Day 30 after PEX.	1 mg/kg/day
Rituxan® (rituximab)	375mg/m^2 IV once weekly for 4 weeks or a reduced dose of 200 mg once weekly for 4 weeks administered immediately after PEX[4]	375 mg/m^2 once weekly

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): Previous severe hypersensitivity reaction to caplacizumab-yhdp or any of the excipients
- Boxed warning(s): None reported

Appendix D: General Information

- Discontinue Cablivi if patient experiences more than 2 recurrences of aTTP while on Cablivi.
- Recurrence is defined as a new decrease (while receiving Cablivi) in the platelet count during the 30-day post daily PEX period that necessitates reinitiation of PEX after normalization of platelet count (≥ 150,000/microL) has occurred.
- Refractory disease is TTP that does not respond to initial treatment with PEX and glucocorticoids (e.g., lack of doubling of the platelet count within four days of initiation, occurrence of new neurologic symptoms not attributable to bleeding or infection).
- A plasma ADAMTS13 activity of < 10 IU/dL (often referred to as 10% of normal ADAMTS13 activity) is the hallmark of TTP. PLASMIC score can be used to estimate the likelihood of severe ADAMTS13 deficiency (< 10%) in adults with suspected TTP (1 point for each) and includes the following parameters:[5]
  - Platelet count < 30,000/microL
  - One or more indicators of hemolysis: reticulocyte count > 2.5%, haptoglobin undetectable, or indirect bilirubin > 2.0 mg/dL [> 34mcmol/L]
  - No active cancer in the preceding year
  - No history of solid organ or hematopoietic stem cell transplant
  - Mean corpuscular volume (MCV) < 90 femtoliters
  - International normalized ratio (INR) < 1.5
  - Creatinine < 2.0 mg/dL [< 177 mcmol/L]

PLASMIC score (points)	Risk of severe ADAMTS13 deficiency
0 to 4	Low Risk (0-4%)
5	Intermediate Risk (5-24%)
6 to 7	High Risk (62-82%)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
aTTP	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 days of treatment during daily plasma exchange: 11 mg subcutaneous injection once daily following plasma exchange. Treatment after plasma exchange period: 11 mg subcutaneous injection once daily continuing for 30 days following the last daily plasma exchange. If after initial treatment course, sign(s) of persistent underlying disease such as suppressed ADAMTS13 activity levels remain present, treatment may be extended for a maximum of 28 days.	Loading: 22 mg/day Maintenance: 11 mg/day

VI. Product Availability

Lyophilized power in a single-dose vial for injection: 11 mg

VII. References

1. Cablivi Prescribing Information. Ghent, Belgium: Ablynx N.V., Inc.; February 2022. Available at: http://products.sanofi.us/cablivi/cablivi.pdf. Accessed January 4, 2023.
2. Scully M, Cataland SR, Peyvandi F, et al. Caplacizumab Treatment for Acquired Thrombotic Thrombocytopenic Purpura. N Engl J Med. 2019 Jan 24:380(4):335-346.
3. Scully M, Hunt BJ, Benjamin S, et al. Guidelines on the diagnosis and management of thrombotic thrombocytopenic purpura and other thrombotic microangiopathies. British Journal of Haematology. 2012 Aug;158(3):323-35.
4. Zheng XL, Vesely SK, Cataland SR, et al. ISTH guidelines for the diagnosis and treatment of thrombotic thrombocytopenic purpura. J Thromb Haemost. 2020 July;18(10):2486-2502.
5. Page EE, Kremer-Hovinga JA, Terrell DR, et al. Rituximab reduces risk for relapse in patients with thrombotic thrombocytopenic purpura. Blood. 2016;127(24):3092
6. Bendapudi PK, Hurwitz S, Fry A, et al. Derivation and external validation of the PLASMIC score for rapid assessment of adults with thrombotic microangiopathies: a cohort study. Lancet Haematology. 2017;4(4):e157.
7. Scully M, de la Rubia J, Pavenski K, et al. Abstract 2080: Long-term safety and efficacy of caplacizumab for acquired thrombotic thrombocytopenic purpura (aTTP): The post-HERCULES study. Presented at 2021 ASH Annual Meeting on December 12, 2021.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
C9047	Injection, caplacizumab-yhdp, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	04/2019	
2Q 2020 annual review: references reviewed and updated.	04/2020	
2Q 2021 annual review: no significant changes; references reviewed and updated.	04/2021	
2Q 2022 annual review: for treatment extension requests, added requirement that member continues to have signs of persistent underlying disease per PI; clarified that requirement for maximum 58 days of therapy per treatment cycle applies to treatment extension requests; added Coding Implications section; references reviewed and updated.	04/2022	
Added alternate pathway for confirmation of diagnosis with ADAMTS13 level with additional information in Appendix D.	07/2022	
2Q 2023 annual review: no significant changes; references reviewed and updated.	04/2023	