Clinical Policy: Caplacizumab-yhdp (Cablivi)

Reference Number: ERX.SPA.325
Effective Date: 06.01.19
Last Review Date: 05.20
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 with a 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);
6. Dose does not exceed (a and b) (*see Section V*):
   a. Loading dose on day 1: 22 mg;
   b. Maintenance: 11 mg per day.

Approval duration: 30 days

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Previously received medication for the covered indication or member has previously met initial approval criteria;
2. Member meets one of the following (a or b):
   a. If request is for a new treatment cycle, member has experienced no more than two recurrences (*see Appendix D*) while taking Cablivi, and Cablivi is prescribed in combination with plasma exchange and immunosuppressive therapy (i.e., glucocorticoids, rituximab);
   b. If request is for treatment extension, 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);
3. Member has received no more than 58 days of Cablivi therapy after completion of plasma exchange therapy;
4. Dose does not exceed the following:
   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: 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 a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – ERX.PA.01 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 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®)	1 mg/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)	375 mg/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 that necessitates reinitiation of plasma exchange 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)
- PLASMIC score for estimating the likelihood of severe ADAMTS13 deficiency in adults with suspected TTP (1 point for each)
  - 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
5	Intermediate Risk
6 to 7	High Risk

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

Single-dose vials for injection: 11 mg/mL

VII. References

1. Cablivi Prescribing Information. Ghent, Belgium: Ablynx N.V., Inc.; February 2019. Available at: http://products.sanofi.us/cablivi/cablivi.pdf. Accessed February 5, 2020.
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. 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

5. 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	03.12.19	05.19
2Q 2020 annual review: no significant changes; references reviewed and updated.	02.05.20	05.20

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.