POLICY: Hematology – Cablivi Utilization Management Medical Policy

- Cablivi® (caplacizumab-yhdp intravenous infusion and subcutaneous injection – Genzyme/Sanofi)

EFFECTIVE DATE: 1/1/2020
LAST REVISION DATE: 02/19/2025

COVERAGE CRITERIA FOR: All UCare Plans

Overview

Cablivi, a von Willebrand factor (vWF)-directed antibody fragment, is indicated for the treatment of **acquired thrombotic thrombocytopenic purpura** (aTTP) in adults, in combination with plasma exchange and immunosuppressive therapy.[1]

Disease Overview

Thrombotic thrombocytopenic purpura (TTP) is a rare but potentially fatal blood disorder.[2-4] TTP may be caused by an inherited severe deficiency of plasma ADAMTS13 (A Disintegrin And Metalloproteinase with ThromboSpondin-1 motif, member 13) activity resulting from mutations; this is referred to as hereditary or congenital TTP. More commonly, TTP is acquired and due to autoantibodies that inhibit plasma ADAMTS13 activity, referred to as immune-mediated (or acquired) TTP (iTTP). Reduced ADAMTS13 activity leads to accumulation of ultra-large vWF multimers in the blood, which bind to platelets and lead to excessive platelet clumping in the microvasculature, resulting in multi-organ failure and death.[2-5] Cablivi is a nanobody that targets the ultra-large vWF and inhibits the interaction between vWF and platelets, thereby preventing vWF platelet adhesion and consumption.[1,5,6]

Dosing Information

Two doses of Cablivi are given on the first day of plasma exchange, followed by one dose of Cablivi per day during plasma exchange; treatment is continued for 30 days after the last plasma exchange session.[1] If, after the initial treatment course, there are signs of persistent underlying disease such as suppressed ADAMTS13 levels, Cablivi therapy may be extended for a maximum of 28 days. Cablivi should be discontinued if the patient experiences more than two recurrences of aTTP while on Cablivi.

Guidelines/Recommendations

The standard of care for treatment of aTTP is plasma exchange and glucocorticoids.[7] Plasma exchange removes the ultra-large vWF and autoantibodies and replenishes ADAMTS13, and immunosuppressants inhibit autoantibody formation. Rituximab can also be added to the aTTP treatment regimen. Rituximab has been shown to reduce the incidence of aTTP relapse by diminishing the production of anti-ADAMTS13 antibodies and restoring ADAMTS13 activity.[2]

The International Society on Thrombosis and Haemostasis (ISTH) formed a multidisciplinary panel including hematologists and pathologists with clinical expertise in the diagnosis and management of TTP, clinicians from other relevant disciplines, and patient representatives to issue recommendations about treatment of TTP (2020).[8] For patients with aTTP or iTTP experiencing an acute event (first event or

relapse), the panel suggests using Cablivi over not using Cablivi. The panel stressed that Cablivi should only be given under the guidance of an experienced clinician, ideally a TTP expert (e.g., a hematologist or pathologist specialized in transfusion medicine with previous experience in treating the disease).

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Cablivi. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for one course of treatment. Note that one course of treatment consists of Cablivi to be administered in conjunction with plasma exchange and Cablivi to be administered for up to 60 days (one dose per day) following the last plasma exchange session. Because of the specialized skills required for evaluation and diagnosis of patients treated with Cablivi as well as the monitoring required for adverse events and long-term efficacy, approval requires Cablivi to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Cablivi is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Acquired Thrombotic Thrombocytopenic Purpura.** Approve for one course of treatment (up to 60 days following the last plasma exchange session) if the patient meets ALL of the following (A, B, C, D, and E):
   - **A)** Patient ≥ 18 years of age; AND
   - **B)** Cablivi was initiated in the inpatient setting, in combination with plasma exchange therapy; AND
   - **C)** Patient is currently receiving at least one immunosuppressive therapy; AND
     Note: Examples include systemic corticosteroids, rituximab (or a rituximab product), cyclosporine, cyclophosphamide, mycophenolate mofetil, hydroxychloroquine, bortezomib.
   - **D)** If the patient has previously received Cablivi, he/she has not had more than two recurrences of acquired thrombotic thrombocytopenic purpura while on Cablivi; AND
   - **E)** The medication is prescribed by or in consultation with a hematologist.

   Dosing. Approve the following dosing regimens:
   - **A)** Day 1 of treatment with plasma exchange: Two doses of Cablivi (11 mg intravenous [IV] bolus prior to plasma exchange followed by an 11 mg subcutaneous [SC] dose after completion of plasma exchange); AND
   - **B)** 11 mg SC injection up to once daily; AND
   - **C)** Do not exceed 60 doses following the last plasma exchange session.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Cablivi is not recommended in the following situations.

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Cablivi® intravenous solution and subcutaneous injection [prescribing information]. Cambridge, MA: Genzyme/Sanofi; April 2024.
2. Coppo P, Cuker A, George JN. Thrombotic thrombocytopenic purpura: toward targeted therapy and precision medicine. *Res Pract Thromb Haemost.* 2019;3:26-37.
3. Subhan M, Scully M. Advances in the management of TTP. *Blood Rev*. 2022;55:100945.
4. Zheng XL, Vesely SK, Cataland SR, et al. International Society on Thrombosis and Haemostasis (ISTH) guidelines for the diagnosis of thrombotic thrombocytopenic purpura. *J Thromb Haemost.* 2020;18:2486-2495.
5. Scully M, Cataland SR, Peyvandi F, et al. Caplacizumab treatment for acquired thrombotic thrombocytopenic purpura. *N Engl J Med.* 2019;380:335-346.
6. Scully M, de la Rubia J, Pavenski K, et al. Long-term follow-up of patients treated with caplacizumab and safety and efficacy of repeat caplacizumab use: post-HERCULES study. *J Thromb Haemost.* 2022;20:2810-2822.
7. 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;158:323-335.
8. Zheng XL, Vesely SK, Cataland SR, et al. International Society on Thrombosis and Haemostasis (ISTH) guidelines for the treatment of thrombotic thrombocytopenic purpura. *J Thromb Haemost*. 2020;18:2496-2502.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	02/22/2023
Annual Revision	No criteria changes.	02/21/2024
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024
Annual Revision	No criteria changes.	02/19/2025
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/15/2025