Drug Coverage Policy

Effective Date.....06/15/2024
Coverage Policy Number.....IP0161
Policy Title..... Cablivi

Hematology – Cablivi

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

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

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).

Medical Necessity Criteria

Cablivi is considered medically necessary when the following criteria are met:

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 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

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

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

References

1. Cablivi® intravenous solution and subcutaneous injection [prescribing information]. Cambridge, MA: Genzyme/Sanofi; February 2022.
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.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	No criteria changes	06/15/2024

The policy effective date is in force until updated or retired.