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Next Review Date **7/1/2024**
Coverage Policy Number **IP0161**

Caplacizumab-yhdp

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Related Coverage Resources

Clotting Factors and Antithrombin – (8007)

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. 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.

Overview

This policy supports medical necessity review for caplacizumab-yhdp (**Cablivi** ®) for injection.

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

Medical Necessity Criteria

Caplacizumab-yhdp (**Cablivi**) **is considered medically necessary when the following are met:**

Acquired Thrombotic Thrombocytopenic Purpura (aTTP). Individual meets **ALL** of the following criteria:
A. 18 years of age or older
B. Initiated in an inpatient setting, in combination with plasma exchange therapy, to treat acquired (autoimmune) thrombotic thrombocytopenic purpura (aTTP)
C. Currently receiving at least **ONE** immunosuppressive therapy

D. If caplacizumab-yhdp (Cablivi) has been previously received, there have NOT been more than two recurrences of aTTP while on Cablivi
E. Medication is prescribed by, or in consultation with, a hematologist

Dosing. The following dosing regimens:
1. Day 1 of treatment with plasma exchange: two doses of Cablivi (11 mg intravenous bolus prior to plasma exchange followed by an 11 mg subcutaneous dose after completion of plasma exchange
2. 11 mg subcutaneous injection up to once daily
3. 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.

Reauthorization Criteria

Continuation of caplacizumab-yhdp (Cablivi) is considered medically necessary for aTTP when the above medical necessity criteria are met AND there is documentation of the following:

Persistent underlying disease (suppressed ADAMTS13 activity levels less than 20-30%; neurologic findings such as seizures, dysarthria, confusion)

Authorization Duration

Initial approval duration: up to 30 days

Reauthorization approval duration: up to an additional 28 days maximum

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven.

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

Background

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] 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. If, after the initial treatment course, there are signs of persistent underlying disease such as suppressed ADAMTS13 (A Disintegrin and Metalloproteinase with ThromboSpondin-1 motif, member 13) 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. Cablivi increases the risk of bleeding; the risk of bleeding is further increased in patients with underlying coagulopathies (e.g., hemophilia, other coagulation factor deficiencies) and in patients receiving Cablivi concomitantly with drugs that affect hemostasis and coagulation.

Disease Overview
Thrombotic thrombocytopenic purpura (TTP) is a rare but potentially fatal blood disorder.[2-5] TTP may be caused by an inherited severe deficiency of plasma ADAMTS13 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 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. Cablivi is a nanobody that targets the ultra-large vWF and inhibits the interaction between vWF and platelets, thereby preventing platelet adhesion.[1-3,6]

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.[2,6,7] Rituximab can also be added to the aTTP treatment regimen.[3] Rituximab has been shown to reduce the incidence of aTTP relapse by diminishing the production of anti-ADAMTS13 antibodies and restoring ADAMTS13 activity.[3,4]

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).

References

1. Cablivi for injection [prescribing information]. Cambridge, MA: Genzyme; February 2022.
2. Duggan S. Caplacizumab: first global approval. *Drugs*. 2018;78:1639-1642.
3. Coppo P, Cuker A, George JN. Thrombotic thrombocytopenic purpura: toward targeted therapy and precision medicine. *Res Pract Thromb Haemost*. 2019;3:26-37.
4. Joly BS, Coppo P, Veyradier A. Thrombotic thrombocytopenic purpura. *Blood.* 2017;129:2836-2846.
5. 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.
6. Scully M, Cataland SR, Peyvandi F, et al. Caplacizumab treatment for acquired thrombotic thrombocytopenic purpura. *N Engl J Med*. 2019;380:335-346.
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.