## Drug Monograph

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|---|---|
| Drug/Drug Class: | **Cablivi® (caplacizumab-yhdp) Injection / Anti-von Willebrand factor** |
| Prepared for: | MO HealthNet |
| Prepared by: | Conduent |

☒ **New Criteria** ☐ **Revision of Existing Criteria**

## Executive Summary

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| **Purpose:** | The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use. |
| **Dosage Forms & Manufacturer:** | Cablivi for intravenous or subcutaneous injection is available as a sterile, preservative-free, lyophilized powder in a single-dose vial containing 11 mg caplacizumab per vial.<br><br>Distributed by: Genzyme Corporation, Cambridge, MA 02142 |
| **Summary of Findings:** | The efficacy of Cablivi was established in HERCULES, a randomized, double-blind study of 145 adult patients with acquired thrombotic thrombocytopenia purpura (aTTP). Patients were randomized to either Cablivi or placebo. Patients in both groups received plasma exchange and immunosuppressive therapy. The primary endpoint was time to platelet count response (platelet count ≥ 150,000/µL followed by cessation of daily plasma exchange within 5 days). Treatment with Cablivi in combination with plasma exchange and immunosuppression resulted in a significantly shorter time to platelet count response vs. plasma exchange and immunosuppression alone (Hazard Ratio = 1.55 [95% CI: 1.10, 2.20]; P = 0.01). |
| **Status Recommendation:** | ☒ Prior Authorization (PA) Required ☐ Open Access<br>☐ Clinical Edit ☐ PDL |
| **Type of PA Criteria:** | ☐ Increased Risk of ADE ☐ Non-Preferred Agent<br>☒ Appropriate Indications ☐ No PA Required |

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## Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payers are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

## Introduction [1]

Acquired thrombotic thrombocytopenia purpura (aTTP) is a rare and life-threatening disorder that causes patients to develop extensive blood clots in the small blood vessels throughout the body. These clots can cut off oxygen and blood supply to the major organs and cause strokes and heart attacks that may lead to brain damage or death. Patients may develop aTTP due to conditions such as cancer, HIV, pregnancy, lupus or infections, or after having surgery, bone marrow transplantation or chemotherapy and may require extensive treatment with daily plasma exchange. It is estimated that aTTP affects < 2,000 adults in the United States each year.

## Dosage Form [2]

Cablivi for intravenous or subcutaneous injection is available as a sterile, preservative-free, lyophilized powder in a single-dose vial containing 11 mg caplacizumab per vial.

## Manufacturer [2]

Distributed by: Genzyme Corporation, Cambridge, MA 02142

## Indication(s) [2]

Cablivi is indicated for the treatment of adult patients with aTTP, in combination with plasma exchange and immunosuppressive therapy.

## Clinical Efficacy [2,3,4] (mechanism of action/pharmacology, comparative efficacy)

Cablivi is a von Willebrand factor (vWF)-directed monoclonal antibody fragment that targets the A1-domain of vWF, inhibiting the interaction between vWF and platelets, reducing both vWF-mediated platelet adhesion and platelet consumption.

Pharmacokinetics:

| | **Cablivi** |
|---|---|
| **Absorption** | Subcutaneous: 90% |
| **Volume of Distribution** | 6.33 L |
| **Metabolism** | Hepatic |
| **Excretion** | Renal |
| **Half-life** | Concentration and target-level dependent |

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Clinical Trials Experience
**HERCULES**

| | |
|---|---|
| **STUDY DESIGN** | Phase III double-blind, randomized, parallel group, multicenter placebo-controlled trial (n = 145) |
| **INCLUSION CRITERIA** | • ≥18 years of age<br>• Clinical diagnosis of aTTP<br>• Required initiation of daily plasma exchange treatment and had received one plasma exchange treatment prior to randomization |
| **EXCLUSION CRITERIA** | • Suspected thrombotic microangiopathies that were not associated with TTP<br>• Congenital TTP |
| **TREATMENT REGIMEN** | Patients were randomized to receive parenteral Cablivi or placebo, in addition to standard-of-care treatment for TTP. Patients received an intravenous loading dose of Caplivi (10 mg) or placebo before the start of the first plasma exchange after randomization. Subsequent 10 mg doses were administered subcutaneously, once daily, until 30 days after the last daily plasma exchange |
| **RESULTS** | The primary outcome was the time to normalization of the platelet count, with discontinuation of daily plasma exchange within 5 days thereafter. The median time to normalization of the platelet count was shorter with Cablivi than with placebo (2.69 days [95% confidence interval {CI}, 1.89 to 2.83] vs. 2.88 days [95% CI, 2.68 to 3.56], P=0.01), and patients who received Cablivi were 1.55 times as likely to have a normalization of the platelet count as those who received placebo. |
| **SAFETY** | The most common adverse event was mucocutaneous bleeding, which was reported in 65% of the patients in the caplacizumab group and in 48% in the placebo group. During the trial treatment period, three patients in the placebo group died. One patient in the Cablivi group died from cerebral ischemia after the end of the treatment period. |

## Contraindications [2]

- Previous severe hypersensitivity reaction to caplacizumab or any of the excipients.

## Warnings and Precautions [2]

- Severe bleeding can occur. The risk of bleeding is increased in patients with underlying coagulopathies. If clinically significant bleeding occurs, interrupt treatment. Withhold Cablivi seven days prior to elective surgery, dental procedures, or other invasive

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interventions.

## Adverse Effects [2]

| Most common, ≥ 2% | Cablivi (n = 106) % | Placebo (n = 110) % |
|---|---|---|
| **Epistaxis** | 29 | 6 |
| **Headache** | 21 | 14 |
| **Gingival Bleeding** | 16 | 3 |
| **Fatigue** | 15 | 9 |
| **Urticaria** | 14 | 6 |
| **Pyrexia** | 13 | 11 |
| **Paresthesia** | 12 | 10 |
| **Dyspnea** | 9 | 5 |
| **Back Pain** | 7 | 4 |
| **Myalgia** | 6 | 2 |
| **Injection Site Hemorrhage** | 6 | 1 |
| **Urinary Tract Infection** | 6 | 4 |
| **Vaginal Hemorrhage** | 5 | 2 |
| **Menorrhagia** | 4 | 1 |
| **Hematuria** | 4 | 3 |
| **Injection Site Pruritus** | 3 | 0 |
| **Abdominal Wall Hematoma** | 3 | 1 |

## Drug Interactions [2]

- Concomitant use of Cablivi with any anticoagulant may increase the risk of bleeding.

## Dosage and Administration [2]

Cablivi should be administered upon initiation of plasma exchange therapy. The recommended dose of Cablivi is as follows:

- 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 remain present, treatment may be extended for a maximum of 28 days.

## Cost

| Generic Name | Brand Name | Manufacturer | Dose | Cost** |
|---|---|---|---|---|
| Caplacizumab | Cablivi | Genzyme | 11 mg vial | $7,300 / vial |

** Wholesale Acquisition Cost

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## Conclusion

Cablivi is the first targeted treatment for aTTP. It works by targeting von Willebrand factor, a protein involved in blood hemostasis. The safety and efficacy of Cablivi were demonstrated in a randomized, double blind clinical trial that enrolled 145 adults with aTTP. Treatment with Cablivi in combination with plasma exchange and immunosuppression resulted in a significantly shorter time to platelet count response vs. plasma exchange and immunosuppression alone. The most common adverse reactions associated with Cablivi use are epistaxis, headache, and gingival bleeding.

## Recommendation

The MO HealthNet Division recommends prior authorization status for this product.

## References


1) FDA approves first therapy for the treatment of adult patients with a rare blood clotting disorder. U.S. Food and Drug Administration. https://www.fda.gov/news-events/press-announcements/fda-approves-first-therapy-treatment-adult-patients-rare-blood-clotting-disorder. Accessed May 28, 2019.
2) Product Information: Cablivi® (caplacizumab-yhdp). Genzyme Corporation, Cambridge, MA 02142.
3) Caplacizumab: Drug Information. Lexi-Drugs. Wolters Kluwer Clinical Drug Information Inc.
4) 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.


Prepared by: Carrie Gatzke PharmD
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