Important note:
Unless otherwise indicated, this policy will apply to all lines of business.
Even though this policy may indicate that a particular service or supply may be considered medically necessary and thus covered, this conclusion is not based upon the terms of your particular benefit plan. Each benefit plan contains its own specific provisions for coverage and exclusions. Not all benefits that are determined to be medically necessary will be covered benefits under the terms of your benefit plan. You need to consult the Evidence of Coverage (EOC) or Summary Plan Description (SPD) to determine if there are any exclusions or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and your plan of benefits, the provisions of your benefits plan will govern. However, applicable state mandates will take precedence with respect to fully insured plans and self-funded non-ERISA (e.g., government, school boards, church) plans. Unless otherwise specifically excluded, Federal mandates will apply to all plans. With respect to Medicare-linked plan members, this policy will apply unless there are Medicare policies that provide differing coverage rules, in which case Medicare coverage rules supersede guidelines in this policy. Medicare-linked plan policies will only apply to benefits paid for under Medicare rules, and not to any other health benefit plan benefits. CMS’s Coverage Issues Manual can be found on the CMS website. Similarly, for Medicaid-linked plans, the Texas Medicaid Provider Procedures Manual (TMPPM) supersedes coverage guidelines in this policy where applicable.

SERVICE: Caplacizumab (Cablivi)

PRIOR AUTHORIZATION: Required.

POLICY: Please review the plan’s EOC (Evidence of Coverage) or Summary Plan Description (SPD) for coverage details.

For Medicare plans, please refer to appropriate Medicare LCD (Local Coverage Determination). If there is no applicable LCD, use the criteria set forth below.

For Medicaid plans, please confirm coverage as outlined in the Texas Medicaid TMPPM.

SWHP/FirstCare may consider caplacizumab-yhdp (Cablivi) medically necessary for treatment of persons with acquired thrombotic thrombocytopenic purpura (aTTP) when the following criteria are met:

- Member is caplacizumab-naïve OR member has not experienced more than 2 recurrences of aTTP, while on caplacizumab; and
- The first dose is administered in the inpatient setting, intravenously, in conjunction with a plasma exchange; and
- Cablivi is being used in combination with plasma exchange; and
- Cablivi is being used in combination with immunosuppressive therapy.
- Treatment will continue during the current episode of disease subcutaneously after the plasma exchange on day one and then daily thereafter for 30 days.

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.

Discontinue Cablivi if the member experiences more than 2 recurrences of aTTP, while on Cablivi.

OVERVIEW:

Acquired thrombotic thrombocytopenic purpura (aTTP) is a rare and serious blood disorder in which blood clots form in small blood vessels throughout the body. These clots can lead to serious medical complications. They often obstruct blood flow to the brain, kidneys, and heart, causing ischemic organ damage. Cognitive deficits, arterial hypertension, depression, and shortened life expectancy are other

Caplacizumab (Cablivi)
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common complications of aTTP. Presenting symptoms of aTTP include a low platelet count, petechiae, purpura, and hemolytic anemia. Patients may also present with fever, fatigue, arrhythmia, and shortness of breath.

Certain medications and autoimmune conditions can trigger the onset of aTTP. Other triggers include a recent pregnancy, infection, or bone marrow transplant. The underlying cause of aTTP is autoantibody-mediated deficiency of the ADAMTS13 enzyme. This enzyme cleaves von Willebrand factor (VWF), a large protein with a key role in blood clot formation. Reduced ADAMTS13 enzyme activity leads to VWF ultra-large multimers, which have a high affinity for platelets, promoting extensive clot formation in small blood vessels throughout the body.

The course of aTTP is variable. Episodes occur suddenly and can last a few days, weeks, or even months. In 90% of cases, the first episode occurs during adulthood. Some patients may suffer only 1 episode during their lifetime, but up to 60% will experience a recurrent episode. The precise U.S. incidence of aTTP is unknown. A recent study estimates that the annual incidence of aTTP is 14.89 per 100,000 adult hospitalizations.

An episode of aTTP is considered a hematologic emergency. The therapy of choice is rapid initiation of daily plasma exchange, with the goal of removing circulating ultra-large VWF multimers and autoantibodies to ADAMTS13, as well as replenishing the circulation with active ADAMTS13. Corticosteroids and rituximab may also be given as an adjunct to plasma exchange.

Even with optimal treatment, mortality rates in patients with aTTP range from 10% to 20. New adjunctive treatments for aTTP are needed to improve associated morbidity and mortality outcomes. Cablivi is a novel therapeutic biologic agent developed to meet this need.

Cablivi is a bivalent single-domain anti-VWF nanobody that inhibits the binding of VWF to platelets to prevent the early stages of blood clot formation. Nanobodies are much smaller than conventional monoclonal antibodies, allowing for more rapid distribution, onset of action and clearance. Cablivi’s mechanism of action is targeted and rapid.

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 treatment during daily plasma exchange: 11 mg subcutaneous injection once daily following plasma exchange.
- Treatment after the plasma exchange period: 11 mg subcutaneous injection once daily for 30 days beyond the last 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.

Cablivi should be discontinued if the patient experiences more than 2 recurrences of aTTP while being treated with Cablivi.

Cablivi is as an adjunctive treatment and will not compete with current standard therapies for aTTP.

SUPPORTING DATA:
MEDICAL COVERAGE POLICY
SERVICE: Caplacizumab (Cablivi)
Policy Number: 255
Effective Date: 09/01/2019
Last Review: 07/25/2019
Next Review Date: 07/25/2020

CODES:

Important note: CODES: Due to the wide range of applicable diagnosis codes and potential changes to codes, an inclusive list may not be presented, but the following codes may apply. Inclusion of a code in this section does not guarantee that it will be reimbursed, and patient must meet the criteria set forth in the policy language.

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REFERENCES:
The following scientific references were utilized in the formulation of this medical policy. SWHP will continue to review clinical evidence related to this policy and may modify it at a later date based upon the evolution of the published clinical evidence. Should additional scientific studies become available and they are not included in the list, please forward the reference(s) to SWHP so the information can be reviewed by the Medical Coverage Policy Committee (MCPC) and the Quality Improvement Committee (QIC) to determine if a modification of the policy is in order.

1. FDA Label: [https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761112s000lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761112s000lbl.pdf)