

POLICY: Hematology – Cablivi® (caplacizumab-yhdp for injection, for intravenous or subcutaneous use)

APPROVAL DATE: 02/20/2019; Selected revision 02/27/2019

OVERVIEW

Cablivi, a von Willebrand factor (vWF)-directed antibody fragment, is indicated for the treatment of adult patients with acquired thrombotic thrombocytopenic purpura (aTTP), in combination with plasma exchange and immunosuppressive therapy.¹ Cablivi is given once a day during plasma exchange and 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 an additional 28 days.

Disease Overview

Acquired thrombotic thrombocytopenic purpura (aTTP) is a rare disease characterized by microangiopathic hemolytic anemia and thrombocytopenia.²⁻⁴ aTTP is caused by autoantibodies directed against ADAMTS13. 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.^{1-3,5}

Guidelines/Recommendations

Cablivi has been incorporated into guidelines. The British Committee for Standards in Hematology, along with other experts, published guidelines for the management of thrombotic thrombocytopenic purpura and related thrombotic microangiopathies in 2012.⁶ Plasma exchange and glucocorticoids are recommended for the management of patients with aTTP. Plasma exchange removes the ultra-large vWF and autoantibodies and replenishes ADAMTS13, and immunosuppressants inhibit autoantibody formation.^{2,5,6} 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}

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(s). 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). 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. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

- 1. Acquired Thrombotic Thrombocytopenic Purpura.** Approve for 3 months if the patient meets the ALL of the following criteria (A, B, and C):
 - A) The patient \geq 18 years of age; AND
 - B) The patient is currently receiving at least one immunosuppressive therapy (e.g., systemic corticosteroids, rituximab [or a rituximab product], cyclosporine [Neoral[®], Sandimmune[®], generics], cyclophosphamide, mycophenolate mofetil, [CellCept[®], Myfortic[®], generics], hydrochloroquine, Velcade[®] [bortezomib for injection]); AND
 - C) Cablivi 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 and 11 mg subcutaneous [SC] dose); AND
- B) 11 mg SC injection once daily for up to 3 months.

Note: Cablivi therapy should be discontinued if the patient experiences more than two recurrences of aTTP while on therapy. Close monitoring for bleeding is recommended due to the potential for increased bleeding risk associated with Cablivi therapy, especially in patients with severe hepatic impairment.

The 3-month approval allows for administration of Cablivi for 30 days following the last daily plasma exchange and for a 28-day extension in patients with persistent underlying disease after the initial treatment course.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

- 1. Other Indications.** Coverage is not recommended for circumstances not listed in the Authorization Criteria (FDA-approved indications and Other Uses with Supportive Evidence). Criteria will be updated as new published data are available.

REFERENCES

1. Cablivi[®] for injection [prescribing information]. Cambridge, MA: Genzyme Corporation; February 2019.
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. 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, 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.

HISTORY

Type of Revision	Summary of Changes*	Approval Date
New policy	--	02/20/2019
Selected revision	Revised criterion “The patient is currently receiving daily plasma exchange and at least one immunosuppressant therapy (e.g., corticosteroids with or without a rituximab product” to “The patient is currently receiving at least one immunosuppressive therapy (e.g., systemic corticosteroids ;with or without a rituximab product)].	02/27/2019