Clinical Policy: Caplacizumab-yhdp (Cablivi)
Reference Number: CP.PHAR.416
Effective Date: 03.12.19
Last Review Date: 05.20
Line of Business: Commercial, HIM, Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Caplacizumab-yhdp (Cablivi®) is a von Willebrand factor (vWF)-directed antibody fragment.

FDA Approved Indication(s)
Cablivi is indicated for the treatment of adult patients with acquired thrombotic thrombocytopenic purpura (aTTP), in combination with plasma exchange and immunosuppressive therapy.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Cablivi is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Acquired Thrombotic Thrombocytopenic Purpura (must meet all):
      1. Diagnosis of aTTP confirmed with a PLASMIC score of 6 to 7 (see Appendix D);
      2. Prescribed by or in consultation with a hematologist;
      3. Age ≥ 18 years;
      4. Prescribed in combination with plasma exchange therapy;
      5. Prescribed in combination with immunosuppressive therapy (i.e., glucocorticoids, rituximab);
         *Prior authorization is required for rituximab
      6. Dose does not exceed (a and b) (see Section V):
         a. Loading dose on Day 1: 11mg pre-plasma exchange and 11mg post-plasma exchange (22 mg total);
         b. Maintenance: 11 mg per day.
   Approval duration: 30 days

   B. Other diagnoses/indications
      1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy
   A. Acquired Thrombotic Thrombocytopenic Purpura (must meet all):
1. Previously received medication for the covered indication or member has previously met initial approval criteria;

2. Member meets one of the following (a or b):
   a. If request is for a new treatment cycle, member has experienced no more than two recurrences (see Appendix D) while taking Cablivi, and Cablivi is prescribed in combination with plasma exchange and immunosuppressive therapy (i.e., glucocorticoids, rituximab);
   b. If request is for treatment extension, member is responding positively to therapy as evidenced by, including but not limited to, improvement in any of the following parameters: increase in platelet counts, reduction in neurological symptoms, or improvements in organ-damage markers (lactate dehydrogenase, cardiac troponin I, and serum creatinine);

3. Member has received no more than 58 days of Cablivi therapy after completion of plasma exchange therapy;

4. Dose does not exceed the following:
   a. For new treatment cycle: loading dose of 22 mg on day 1, followed by maintenance dose of 11 mg per day;
   b. For treatment extension: 11 mg per day.

Approval duration: up to a total duration of 58 days post plasma-exchange

B. Other diagnoses/indications (must meet 1 or 2):
   1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
      Approval duration: Duration of request or 6 months (whichever is less); or
   2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:
   A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
   aTTP: acquired thrombotic thrombocytopenic purpura
   FDA: Food and Drug Administration
   FFP: fresh frozen plasma
   PEX: plasma exchange
   vWF: von Willebrand factor

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.
### Drug Name

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma Exchange (PEX)</td>
<td>1 to 1.5x estimated plasma volume daily until two days after normalization of platelet count (≥ 150 x 10⁹/L).</td>
<td>1 to 1.5x estimated plasma volume</td>
</tr>
<tr>
<td>• Fresh Frozen Plasma (FFP)</td>
<td>1 to 1.5x estimated plasma volume</td>
<td></td>
</tr>
<tr>
<td>• Solvent detergent/viral-inactivated plasma</td>
<td>1 to 1.5x estimated plasma volume</td>
<td></td>
</tr>
<tr>
<td>• Cryosupernatant</td>
<td>1 to 1.5x estimated plasma volume</td>
<td></td>
</tr>
<tr>
<td>methylprednisolone (Solu-Medrol&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>1 mg/kg/day IV or PO during PEX and continued for 1 week after PEX. Tapered with the goal of being corticosteroid-free by Day 30 after PEX.</td>
<td>1 mg/kg/day</td>
</tr>
<tr>
<td>Rituxan&lt;sup&gt;®&lt;/sup&gt; (rituximab)</td>
<td>375 mg/m² IV once weekly for 4 weeks or a reduced dose of 200 mg once weekly for 4 weeks administered immediately after PEX</td>
<td>375 mg/m² once weekly</td>
</tr>
</tbody>
</table>

Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.

### Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): Previous severe hypersensitivity reaction to caplacizumab-yhdp or any of the excipients
- Boxed warning(s): None reported

### Appendix D: General Information
- Discontinue Cablivi if patient experiences more than 2 recurrences of aTTP while on Cablivi.
- Recurrence is defined as a new decrease (while receiving Cablivi) in the platelet count that necessitates reintiation of plasma exchange after normalization of platelet count (≥ 150,000/microL) has occurred.
- Refractory disease is TTP that does not respond to initial treatment with PEX and glucocorticoids (e.g., lack of doubling of the platelet count within four days of initiation, occurrence of new neurologic symptoms not attributable to bleeding or infection).
- PLASMIC score for estimating the likelihood of severe ADAMTS13 deficiency in adults with suspected TTP (1 point for each)<sup>5</sup>
  - Platelet count < 30,000/microL
  - One or more indicators of hemolysis: reticulocyte count > 2.5%, haptoglobin undetectable, or indirect bilirubin > 2.0 mg/dL [< 34 mcmol/L]
  - No active cancer in the preceding year
  - No history of solid organ or hematopoietic stem cell transplant
  - Mean corpuscular volume (MCV) < 90 femtoliters
  - International normalized ratio (INR) < 1.5
  - Creatinine < 2.0 mg/dL [≤ 177 mcmol/L]

<table>
<thead>
<tr>
<th>PLASMIC score (points)</th>
<th>Risk of severe ADAMTS13 deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 to 4</td>
<td>Low Risk</td>
</tr>
<tr>
<td>5</td>
<td>Intermediate Risk</td>
</tr>
</tbody>
</table>

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V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>aTTP</td>
<td><strong>First day of treatment:</strong> 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. <strong>Subsequent days of treatment during daily plasma exchange:</strong> 11 mg subcutaneous injection once daily following plasma exchange. <strong>Treatment after plasma exchange period:</strong> 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 such as suppressed ADAMTS13 activity levels remain present, treatment may be extended for a maximum of 28 days.</td>
<td>Loading: 22 mg/day Maintenance: 11 mg/day</td>
</tr>
</tbody>
</table>

VI. Product Availability

Single-dose vials for injection: 11 mg/mL

VII. References


Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Policy created.</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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<tbody>
<tr>
<td>Policy created.</td>
<td>03.12.19</td>
<td>05.19</td>
</tr>
<tr>
<td>Finalized line of businesses on policy to include HIM per SDC and prior clinical guidance.</td>
<td>10.07.19</td>
<td></td>
</tr>
<tr>
<td>2Q20 annual review: no significant changes; references reviewed and updated.</td>
<td>02.05.20</td>
<td>05.20</td>
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</table>
Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.