Clinical Policy: Ocrelizumab (Ocrevus)
Reference Number: CP.CPA.307
Effective Date: 04.11.17
Last Review Date: 05.19
Line of Business: Commercial

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

Description
Ocrelizumab (Ocrevus™) is a CD20-directed cytolytic antibody.

FDA Approved Indication(s)
Ocrevus is indicated for the treatment of patients with relapsing or primary progressive forms of multiple sclerosis (MS).

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 Ocrevus is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Multiple Sclerosis (must meet all):
      1. Diagnosis of relapsing-remitting or primary progressive MS;
      2. Prescribed by or in consultation with a neurologist;
      3. Age ≥ 18 years;
      4. If relapsing-remitting MS, failure of two of the following at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced: Aubagio®, Tecfidera®, Gilenya™, Avonex®, Betaseron®, Plegridy®, glatiramer, Copaxone®, Glatopa®, or Rebif®;
      *Prior authorization is required for all disease modifying therapies for MS
      5. Ocrevus is not prescribed concurrently with other disease modifying therapies for MS (see Appendix D);
      6. At the time of request, member does not have active hepatitis B infection (positive results for hepatitis B surface antigen and anti-hepatitis B virus tests);
      7. Dose does not exceed the following:
         a. Initial dose: 300 mg, followed by a second 300 mg dose 2 weeks later;
         b. Maintenance dose: 600 mg every 6 months.
      Approval duration: 6 months or to the member’s renewal date, whichever is longer

   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.
II. Continued Therapy
   A. Multiple Sclerosis (must meet all):
      1. Currently receiving medication via Centene benefit or member has previously met
         initial approval criteria;
      2. Member is responding positively to therapy;
      3. Ocrevus is not prescribed concurrently with other disease modifying therapies for MS
         (see Appendix D);
      4. If request is for a dose increase, new dose does not exceed 600 mg every 6 months.
      Approval duration: 6 months or to the member’s renewal date, whichever is longer
   
   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.

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 policy –
      CP.CPA.09 for commercial or evidence of coverage documents.

IV. Appendices/General Information

   Appendix A: Abbreviation/Acronym Key
   FDA: Food and Drug Administration
   MS: multiple sclerosis

   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 and may require prior
   authorization.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/ Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avonex®, Rebif® (interferon beta-1a)</td>
<td>Avonex: 30 mcg IM Q week, Rebif: 22 mcg or 44 mcg SC TIW</td>
<td>Avonex: 30 mcg/week, Rebif: 44 mcg TIW</td>
</tr>
<tr>
<td>Plegridy® (peginterferon beta-1a)</td>
<td>125 mcg SC Q2 weeks</td>
<td>125 mcg/2 weeks</td>
</tr>
<tr>
<td>Betaseron®, Extavia® (interferon beta-1b)</td>
<td>250 mcg SC QOD</td>
<td>250 mg QOD</td>
</tr>
<tr>
<td>glatiramer acetate (Copaxone®, Glatopa®)</td>
<td>20 mg SC QD or 40 mg SC TIW</td>
<td>20 mg/day or 40 mg TIW</td>
</tr>
<tr>
<td>Aubagio® (teriflunomide)</td>
<td>7 mg or 14 mg PO QD</td>
<td>14 mg/day</td>
</tr>
<tr>
<td>Gilenya™ ( fingolimod)</td>
<td>0.5 mg PO QD</td>
<td>0.5 mg/day</td>
</tr>
<tr>
<td>Drug Name</td>
<td>Dosing Regimen</td>
<td>Dose Limit/Maximum Dose</td>
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<tr>
<td>Tecfidera® (dimethyl fumarate)</td>
<td>120 mg PO BID for 7 days, followed by 240 mg PO BID</td>
<td>480 mg/day</td>
</tr>
</tbody>
</table>

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

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): active hepatitis B virus infection; history of life-threatening infusion reaction to Ocrevus
- Boxed warning(s): none reported

Appendix D: General Information
- Disease-modifying therapies for MS are: glatiramer acetate (Copaxone®, Glatopa®), interferon beta-1a (Avonex®, Rebif®), interferon beta-1b (Betaseron®, Extavia®), peginterferon beta-1a (Plegridy®), dimethyl fumarate (Tecfidera®), fingolimod (GilenyaTM), teriflunomide (Aubagio®), alemtuzumab (Lemtrada®), mitoxantrone (Novantrone®), natalizumab (Tysabri®), and ocreliuzmab (OcrevusTM).

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relapsing and primary progressive MS</td>
<td>Initial 300 mg intravenous infusion with a second 300 mg intravenous infusion two weeks later, followed by subsequent doses of 600 mg via intravenous infusion every 6 months</td>
<td>600 mg/6 months</td>
</tr>
</tbody>
</table>

VI. Product Availability
- Single-dose vial: 300 mg/10 mL

VII. References
## Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
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<tbody>
<tr>
<td>New policy.</td>
<td>04.17</td>
<td>04.17</td>
</tr>
<tr>
<td>Removed requirement of MRI to confirm diagnosis</td>
<td>10.18.17</td>
<td></td>
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<tr>
<td>2Q 2018 annual review: added age; added redirection in line with clinical guidance; approval durations modified to 6 months or to the member’s renewal date; references reviewed and updated.</td>
<td>01.05.18</td>
<td>05.18</td>
</tr>
<tr>
<td>2Q 2019 annual review: no significant changes; added glatiramer as a step-through option; references reviewed and updated.</td>
<td>02.06.19</td>
<td>05.19</td>
</tr>
</tbody>
</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.

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