Clinical Policy: Ocrelizumab (Ocrevus)
Reference Number: CP.PHAR.335
Effective Date: 05.01.17
Last Review Date: 08.20
Line of Business: Commercial, HIM, Medicaid

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:

- Relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults
- Primary progressive MS, in adults

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 one of the following (a, b, c, or d):
         a. Clinically isolated syndrome, and member is contraindicated to both or has experienced clinically significant adverse effects to one of the following at up to maximally indicated doses: an interferon-beta agent (Avonex®, Betaseron®, Rebif®, or Plegridy®), glatiramer (Copaxone®, Glatopa®);
         b. Relapsing-remitting MS, and failure of two of the following at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated: Aubagio®, Tecfidera®, Gilenya™, an interferon-beta agent (Avonex, Betaseron, Rebif, or Plegridy), glatiramer (Copaxone®, Glatopa®), Mayzent®;  
            *Prior authorization is required for all disease modifying therapies for MS
         c. Secondary progressive MS
         d. Primary progressive MS;
      2. Prescribed by or in consultation with a neurologist;
      3. Age ≥ 18 years;
      4. Ocrevus is not prescribed concurrently with other disease modifying therapies for MS (see Appendix D);
      5. Documentation of baseline number of relapses per year and expanded disability status scale (EDSS) score;
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:
Medicaid/HIM – 6 months
Commercial – 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, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 meets one of the following (a or b):
      a. If member has received < 1 year of total treatment: Member is responding positively to therapy;
      b. If member has received ≥ 1 year of total treatment: Member meets one of the following (i, ii, iii, or iv):
         i. Member has not had an increase in the number of relapses per year compared to baseline;
         ii. Member has not had ≥ 2 new MRI-detected lesions;
         iii. Member has not had an increase in EDSS score from baseline;
         iv. Medical justification supports that 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:
Medicaid/HIM – first re-authorization: 6 months; second and subsequent re-authorizations: 12 months
Commercial – 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, 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 policy – 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
EDSS: expanded disability status scale
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 for all relevant lines of business 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>Aubagio® (teriflunomide)</td>
<td>7 mg or 14 mg PO QD</td>
<td>14 mg/day</td>
</tr>
<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® (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>Gilenya™ (fingolimod)</td>
<td>0.5 mg PO QD</td>
<td>0.5 mg/day</td>
</tr>
<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>
<tr>
<td>Mayzent® (siponimod)</td>
<td>All patients:</td>
<td>2 mg/day</td>
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<tr>
<td></td>
<td>Day 1 and 2: 0.25 mg PO QD</td>
<td></td>
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<tr>
<td></td>
<td>Day 3: 0.5 mg PO QD</td>
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<tr>
<td></td>
<td>Day 4: 0.75 mg PO QD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>*CYP2C9 genotypes *1/*1, *1/*2, or *2/*2: Day 5: 1.25 mg PO QD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day 6 and onward: 2 mg PO QD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>*CYP2C9 genotypes *1/*3 or *2/*3: Day 5 and onward: 1 mg PO QD</td>
<td></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®), diroximel fumarate (Vumerity™), monomethyl fumarate (Bafiertam™), fingolimod (GilenyaTM), teriflunomide (Aubagio®), alemtuzumab (Lemtrada®), mitoxantrone (Novantrone®), natalizumab (Tysabri®), ocrelizumab (Ocrevus™), cladribine (Mavenclad®), siponimod (Mayzent®), and ozanimod (Zeposia®).
- Of the disease-modifying therapies for MS that are FDA-labeled for CIS, only the interferon products, glatiramer, and Aubagio have demonstrated any efficacy in decreasing the risk of conversion to MS compared to placebo. This is supported by the AAN 2018 MS guidelines.

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 IV infusion with a second 300 mg IV infusion two weeks later, followed by subsequent doses of 600 mg via IV 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>
</thead>
<tbody>
<tr>
<td>Changed requirement of failure of glatiramer acetate, Tecfidera, or Gilenya, to the following: Tecfidera or Gilenya and either an interferon-beta agent or glatiramer; or Tecfidera and Gilenya.</td>
<td>05.17</td>
<td></td>
</tr>
<tr>
<td>Age requirement added. Removed MRI requirement. Removed “Appendix B- general information.”</td>
<td>07.17</td>
<td>08.17</td>
</tr>
<tr>
<td>2Q 2018 annual review: no significant changes; references reviewed and updated.</td>
<td>01.05.18</td>
<td>05.18</td>
</tr>
<tr>
<td>2Q 2019 annual review: no significant changes; specified that generic forms of glatiramer are preferred; references reviewed and updated.</td>
<td>02.06.19</td>
<td>05.19</td>
</tr>
<tr>
<td>RT4: added coverage for CIS and SPMS per updated FDA labeling; references reviewed and updated.</td>
<td>08.02.19</td>
<td></td>
</tr>
<tr>
<td>Updated RRMS re-directions and added CIS re-directions per SDC and prior clinical guidance; added COM and HIM lines of business (CP.CPA.307 and HIM.PA.SP31 retired)</td>
<td>01.21.20</td>
<td></td>
</tr>
<tr>
<td>2Q 2020 annual review: modified CIS re-direction to include glatiramer to per SDC; references reviewed and updated.</td>
<td>01.27.20</td>
<td>05.20</td>
</tr>
<tr>
<td>Added requirements for documentation of baseline relapses/EDSS and objective measures of positive response upon re-authorization; modified Medicaid/HIM continued approval duration to 6 months for the first re-authorization and 12 months for second/subsequent re-authorizations; references reviewed and updated.</td>
<td>05.27.20</td>
<td>08.20</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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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.

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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.

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