RXADVANCE
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Clinical Policy Title:	ocrelizumab
Policy Number:	RxA.423
Drug(s) Applied:	Ocrevus™
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of business

Background

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Ocrelizumab (Ocrevus™)	Relapsing and primary progressive MS	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	600 mg/6 months

Dosage Forms

- Single-dose vial: 300 mg/10 mL

Clinical Policy

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

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 contraindicated or clinically significant adverse effects are experienced: Aubagio®, Tecfidera®, Gilenya™, Avonex®, Betaseron®, Plegridy®, glatiramer, Mayzent®, Copaxone®, Glatopa®, or Rebif®;
**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. 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);
6. 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
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Multiple Sclerosis (must meet all)**:**

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy.
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
Commercial: 6 months
Medicaid: 6 months

III. Appendices

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.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Aubagio® (teriflunomide	7 mg or 14 mg PO once daily	14 mg/day

Avonex®, Rebif® (interferon beta-1a)	Avonex: 30 mcg IM Q week Rebif: 22 mcg or 44 mcg SC TIW	Avonex: 30 mcg/week Rebif: 44 mcg TIW
Plegridy® (peginterferon beta-1a)	125 mcg SC Q2 weeks	125 mcg/2 weeks
Betaseron®, Extavia® (interferon beta-1b)	250 mcg SC QOD	250 mg QOD
glatiramer acetate (Copaxone®, Glatopa®)	20 mg SC once daily or 40 mg SC TIW	20 mg/day or 40 mg TIW
Gilenya™ (fingolimod)	0.5 mg PO once daily	0.5 mg/day
Tecfidera® (dimethyl fumarate)	120 mg PO BID for 7 days, followed by 240 mg PO BID	480 mg/day
Mayzent® (siponimod)	All patients: Day 1 and 2: 0.25 mg PO once daily Day 3: 0.5 mg PO once daily Day 4: 0.75 mg PO once daily CYP2C9 genotypes *1/*1, *1/*2, or *2/*2: Day 5: 1.25 mg PO once daily Day 6 and onward: 2 mg PO once daily CYP2C9 genotypes *1/*3 or *2/*3: Day 5 and onward: 1 mg PO once daily	2 mg/day

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 (Gilenya™), teriflunomide (Aubagio®), alemtuzumab (Lemtrada®), mitoxantrone (Novantrone®), natalizumab (Tysabri®), ocrelizumab (Ocrevus™), cladribine (Mavenclad®), and siponimod (Mayzent®).
- Although many disease-modifying therapies for MS 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.

References

1. Ocrevus Prescribing Information. South San Francisco, CA: Genentech, Inc; May 2020. Available at www.ocrevus.com. Accessed July 21, 2020.
2. Costello K, Halper J, Kalb R, Skutnik L, Rapp R. The use of disease-modifying therapies in multiple sclerosis, principles and current evidence – a consensus paper by the Multiple Sclerosis Coalition. March 2017. Accessed July 21, 2020.
3. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: disease-modifying therapies for adults with multiple sclerosis: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2018; 90(17): 777-788. Full guideline available at: https://www.aan.com/Guidelines/home/GetGuidelineContent/904.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed 1. Clinical Policy title was updated. 2. Lines of business 'Policy Applies to' was updated to 'All lines of business'. 3. Appendix B(Therapeutic alternatives): Mayzent® (siponimod) 4. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 5. Reference reviewed and updated.	07/21/2020	09/14/2020