Clinical Policy Title:	ocrelizumab
Policy Number:	RxA.423
Drug(s) Applied:	Ocrevus®
Original Policy Date:	03/06/2020
Last Review Date:	07/18/2022
Line of Business Policy Applies to:	All lines of business

Background

Ocrelizumab (Ocrevus®) is a CD20-directed cytolytic antibody. It 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 (30 mg/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. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Multiple Sclerosis (must meet all):

1. Diagnosis of relapsing multiple sclerosis (RMS), including clinically isolated syndrome, or relapsing remitting disease, or active secondary progressive disease;
2. Diagnosis of primary progressive MS;
3. For RMS trial and failure of at least one (1) preferred disease modifying therapies (Avonex®, Betaseron®, Copaxone®, Vumerity®, Bafiertam®, or Kesimpta®), at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;

*Prior authorization is required for all disease modifying therapies for MS.

4. Prescribed by or in consultation with a neurologist;
5. Age ≥ 18 years;
6. Ocrevus® is not prescribed concurrently with other disease modifying therapies for MS (see Appendix D);
7. 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);
8. Prior to initiating Ocrevus®, perform testing for quantitative serum immunoglobulin (for patients with low serum immunoglobulins, consult immunology experts before initiating treatment with Ocrevus®);
9. 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. Member is currently receiving medication that has been authorized by RxAdvance or the member has 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: 12 months
Medicaid: 12 months

III. Appendices

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

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Aubagio®	7 mg or 14 mg orally once daily	14 mg/day
Avonex®, Rebif®	Avonex: 30 mcg intramuscularly every week Rebif: 22 mcg or 44 mcg subcutaneously three times weekly	Avonex: 30 mcg/week Rebif: 44 mcg three times weekly
Plegridy®	125 mcg subcutaneously every 2 weeks	125 mcg/2 weeks

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Betaseron®, Extavia®	250 mcg subcutaneously every other day	250 mg every other day
glatiramer acetate (Copaxone®, Glatopa®)	20 mg subcutaneously once daily or 40 mg subcutaneously three times weekly	20 mg/day or 40 mg Three times weekly
Gilenya®	0.5 mg orally once daily	0.5 mg/day
dimethyl fumarate (Tecfidera®)	120 mg orally twice daily for 7 days, followed by 240 mg orally twice daily	480 mg/day
Mayzent®	All patients: Day 1 and 2: 0.25 mg orally once daily Day 3: 0.5 mg orally once daily Day 4: 0.75 mg orally once daily CYP2C9 genotypes *1/*1, *1/*2, or *2/*2: Day 5: 1.25 mg orally once daily Day 6 and onward: 2 mg orally once daily CYP2C9 genotypes *1/*3 or *2/*3: Day 5 and onward: 1 mg orally once daily	2 mg/day
Zeposia®	Initial dose: Days 1 -4: 0.23 mg once daily Days 5-7: 0.46 mg once daily Day 8 and thereafter: 0.92 mg once daily Maintenance: 0.92 mg taken orally once daily starting on Day 8	0.92 mg once daily
Bafiertam™	Starting dose: 95 mg twice a day, orally, for 7 days Maintenance dose: after 7 days: 190 mg (administered as two 95 mg capsules) twice a day, orally	300 mg/day
Ponvory™	A starter pack must be used for patients initiating treatment with Ponvory™.	20 mg orally once daily
	Initiate treatment with a 14-day titration: Titration day: Daily dose Days 1 and 2: 2 mg Days 3 and 4: 3 mg Days 5 and 6: 4 mg Days 7: 5 mg Day 8: 6 mg	

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Day 9: 7 mg Day 10: 8 mg Day 11: 9 mg Day 12, 13 and 14: 10 mg Maintenance: 20 mg once daily, beginning on day 15	

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Active hepatitis B virus infection; history of life-threatening infusion reaction to Ocrevus®.

*Contraindications listed reflect direct statements made in the manufacturer's package insert; for additional uses, warnings, and precautions, please refer to clinical guidelines.

- 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-labelled 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; March 2021. Available at www.ocrevus.com. Accessed March 25, 2022.
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. Available at: https://ms-coalition.org/wp-content/uploads/2019/06/MSC_DMTPaper_062019.pdf. Accessed March 25, 2022.
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. Accessed March 25, 2022.
4. Ocrelizumab. Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed March 25, 2022.
5. Clinical Pharmacology [database online] powered by Clinical Key. Tampa, FL: Elsevier, 2021. Accessed with subscription at: http://www.clinicalkey.com. Accessed March 25, 2022.

Review/Revision History	Review/Revision 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
Policy was reviewed: 1. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 2. Initial Approval Criteria I.A.1.b was updated to changed from trial and failure of "two" alternative drugs to trial and failure of "at least one" alternative drug; list of acceptable drugs to try was updated from "Aubagio®, Tecfidera®, Gilenya®, Avonex®, Betaseron®, Plegridy®, glatiramer, Mayzent®, Copaxone®, Glatopa®, or Rebif®" to "Avonex®, Betaseron®, Copaxone®, Vumerity®, Bafiertam®, Kesimpta®". 3. Initial therapy criteria was updated to add 'testing of quantitative serum immunoglobulin prior to initiating Ocrevus' I.A.6. 4. Continued Therapy criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance..." 5. Approval duration for Continued therapy criteria was updated from 6 months to 12 months. 6. Appendix B: Therapeutic alternative verbiage was updated to "Below are suggested therapeutic alternatives based on clinical guidance.." 7. Appendix B was updated to add "Zeposia", "Bafiertam" and "Ponvory" as therapeutic alternatives.	06/25/2021	09/14/2021

8. Statement about drug listing format in Appendix B is updated to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 9. References were reviewed and updated.		
Policy was reviewed: 1. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 2. Disclaimer about contraindications "Contraindications listed reflect statements made in the manufacturer's package insert..." was added to Appendix C. 3. Appendix D: Updated to remove statement Although many disease-modifying therapies for MS are FDA-labelled 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. 4. References were reviewed and updated.	03/25/2022	07/18/2022