Effective Date: 08/01/2017
Last P&T Approval/Version: 04/27/2022
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Policy Number: C11250-A

Ocrevus (ocrelizumab)

PRODUCTS AFFECTED

Ocrevus (ocrelizumab)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive

DIAGNOSIS:
Multiple Sclerosis

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review

A. RELAPSING FORMS OF MULTIPLE SCLEROSIS:
1. Documentation of a definitive diagnosis of a relapsing form of multiple sclerosis as defined by the McDonald criteria (see Appendix), including: Relapsing- remitting multiple sclerosis [RRMS], secondary-progressive multiple sclerosis [SPMS] with relapses, and progressive-relapsing multiple sclerosis [PRMS] or First clinical episode with MRI features consistent with multiple sclerosis
AND
2. Documentation of screening for hepatitis B virus AND for patients who are negative for surface antigen [HBsAg] and positive for HB core antibody [HBcAb+] or are carriers of HBV [HBsAg+], documentation of a consult with a liver disease experts before starting treatment

AND

3. Member is not currently being treated with a disease modifying agent (DMA) other than the requested agent, B cell targeted therapy (e.g. rituximab, belimumab, ofatumumab), or lymphocyte trafficking blocker (e.g. alemtuzumab, mitoxantrone)
   AND
4. (a) Documentation of **inadequate response (trial of 3 months) to ONE of the following: ONE of Interferon therapy (Avonex, Rebif, Extavia, Betaseron, Plegridy) OR Glatiramer OR Aubagio (teriflunomide), Tecfidera (dimethyl fumerate), Gilenya (fingolimod)
   **Inadequate response is defined as meeting at least TWO (2) of the following three criteria during treatment: 1) Clinical relapses (at least two relapses within the past 12 months), 2) CNS lesions progression as measured by MRI, OR 3) Worsening disability (e.g. sustained worsening of EDSS score or neurological exam findings; worsening disability include, but not limited to, decreased mobility, decreased ability to perform activities of daily living due to disease progression, or EDSS > 3.5)
   OR
   (b) Documentation member has indicators of a highly active course of multiple sclerosis: (i) age of MS onset ≥ 40 years of age, (ii) male gender, (iii) African American, (iv) motor, sphincter, brainstem-cerebellar symptoms, (v) MRI lesions in brainstem or spina cord, OR (vi)
   ≥ 2 acute relapses in first 2 years of onset with significant sustained disability following relapse AND
5. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to OCREVUS (ocrelizumab) include: Active hepatitis B virus infection]
   AND
6. IF REQUEST IS FOR A NON-FORMULARY PRODUCT: Documentation of trial/failure of, OR Intolerance to a majority (not more than 3) of the preferred formulary/PDL alternatives for the given diagnosis. If yes, please submit documentation including medication(s) tried, dates of trial(s) and reason for **treatment failure(s).
   **May be defined as meeting at least TWO (2) of the following three criteria during treatment: 1) Clinical relapses (at least two relapses within the past 12 months), 2) CNS lesions progression as measured by MRI, OR 3) Worsening disability (e.g. sustained worsening of EDSS score or neurological exam findings; worsening disability include, but not limited to, decreased mobility, decreased ability to perform activities of daily living due to disease progression, or EDSS > 3.5)

B. PRIMARY PROGRESSIVE MULTIPLE SCLEROSIS:

1. Documentation of a diagnosis of primary progressive multiple sclerosis (PPMS)
   AND
2. Documentation of screening for hepatitis B virus AND for patients who are negative for surface antigen [HBsAg] and positive for HB core antibody [HBcAb+] or are carriers of HBV [HBsAg+], documentation of a consult with a liver disease expert before starting treatment
   AND
3. Member is not currently being treated with a disease modifying agent (DMA) other than the requested agent, B cell targeted therapy (e.g. rituximab, belimumab, ofatumumab), or lymphocyte trafficking blocker (e.g. alemtuzumab, mitoxantrone)
   AND
4. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to OCREVUS (ocrelizumab) include: Active hepatitis B virus infection]

CONTINUATION OF THERAPY:

A. RELAPSING FORM OF MULTIPLE SCLEROSIS:

1. (a) Documentation of a stable number or decrease in acute attacks (relapses) within the last 6 months
   OR
   (b) Documentation of lack of progression or sustained disability
   OR
   (c) Recent (within last 6 months) MRI shows lack of development of new asymptomatic lesions
   AND
2. Documentation member has been adherent to therapy at least 85% of the time as verified by Prescriber and member's medication fill history
   AND
3. Member had not experienced any intolerable adverse effects or drug toxicity

B. PRIMARY PROGRESSIVE MULTIPLE SCLEROSIS:

1. (a) Documentation of lack of progression or sustained disability
   OR
   (b) Recent (within last 6 months) MRI shows lack of development of new asymptomatic lesions
   AND
2. Documentation member has been adherent to therapy at least 85% of the time as verified by Prescriber and member's medication fill history
   AND
3. Member had not experienced any intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:
Initial Authorization: 12 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a board-certified neurologist or a multiple sclerosis specialist. Please submit consultation notes if prescribed after consultation

AGE RESTRICTIONS:
18 years of age or older

QUANTITY:
TWO 300 mg doses per 6 months (to occur in the first month) then ONE 600 mg dose per 6 months

PLACE OF ADMINISTRATION:
The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.

Note: Site of Care Utilization Management Policy applies for Ocrevus (ocrelizumab). For information on site of care, see
Specialty Medication Administration Site of Care Coverage Criteria (molinamarketplace.com)

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intravenous

DRUG CLASS:
Multiple Sclerosis Agents - Monoclonal Antibodies

FDA-APPROVED USES:
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

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
APPENDIX: Summary of 2017 McDonald Criteria for the Diagnosis of MS

CLINICAL PRESENTATION	ADDITIONAL CRITERIA TO MAKE MS DIAGNOSIS
...in a person who has experienced a typical attack/CIS at onset	
• 2 or more attacks and clinical evidence of 2 or more lesions; OR • 2 or more attacks and clinical evidence of 1 lesion with clear historical evidence of prior attack involving lesion in different location	None. DIS and DIT have been met.
• 2 or more attacks and clinical evidence of 1 lesion	DIS shown by one of these criteria: - additional clinical attack implicating different CNS site - 1 or more MS-typical T2 lesions in 2 or more areas of CNS: periventricular, cortical, juxtacortical, infratentorial or spinal cord
• 1 attack and clinical evidence of 2 or more lesions	DIT shown by one of these criteria: - Additional clinical attack - Simultaneous presence of both enhancing and non-enhancing MS-typical MRI lesions, or new T2 or enhancing MRI lesion compared to baseline scan (without regard to timing of baseline scan) - CSF oligoclonal bands
• 1 attack and clinical evidence of 1 lesion	DIS shown by one of these criteria: - Additional attack implicating different CNS site - 1 or more MS-typical T2 lesions in 2 or more areas of CNS: periventricular, cortical, juxtacortical, infratentorial or spinal cord **AND** DIT shown by one of these criteria: - additional clinical attack - Simultaneous presence of both enhancing and non-enhancing MS-typical MRI lesions, or new T2 or enhancing MRI lesion compared to baseline scan (without regard to timing of baseline scan) - CSF oligoclonal bands
...in a person who has steady progression of disease since onset	
1 year of disease progression (retrospective or prospective)	DIS shown by at least two of these criteria: - 1 or more MS-typical T2 lesions (periventricular, cortical, juxtacortical or infratentorial) - 2 or more T2 spinal cord lesions - CSF oligoclonal bands

DIT = Dissemination in time
DIS = Dissemination in space
CNS = central nervous system
T2 lesion = hyperintense lesion on T2-weighted MRI
CSF = cerebrospinal fluid

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Ocrevus is a CD20-directed cytolytic antibody indicated for the treatment of patients with relapsing or primary progressive forms of multiple sclerosis (MS).1 The efficacy of Ocrevus in patients with relapsing MS was established in two identical, Phase III, multicenter, randomized, double-blind, double-dummy, active controlled, published, parallel group trials (OPERA I and OPERA II), that used Rebif® (interferon beta-1a subcutaneous [SC]) as an active comparator for up to 96 weeks.2 Approximately 25% of patients had previously used MS disease-modifying therapy (mainly beta interferon or glatiramer acetate products). In these two trials (OPERA I n = 821 and OPERA II n =825) the annualized relapse rate (ARR) among patients with relapsing MS was lower with Ocrevus in both studies compared with Rebif (0.16 vs. 0.29; P < 0.001). In a prespecified analysis the percentage of patients with disability progression confirmed at 12 weeks was significantly lower with Ocrevus compared with Rebif (9.1% vs. 13.6%; P < 0.001), as well as the percentage of patients with disability progression confirmed at 24 weeks (6.9% vs. 10.5%; P = 0.001). Several magnetic resonance imaging (MRI) parameters were also more favorable with Ocrevus vs. Rebif. The percentage of patients with no evidence of disease activity by Week 96, an exploratory endpoint, was also statistically significantly larger for patients given Ocrevus vs. Rebif (47.9% vs. 29.2%; P < 0.001). The efficacy of Ocrevus in patients with primary progressive MS was established in one Phase III, randomized, parallel-group, double-blind, placebo-controlled published trial (ORATORIO [n = 732]).3 Therapy duration was at least
120 weeks. Most patients (88%) had not previously used MS disease-modifying therapy. In ORATORIO the primary endpoint was the percentage of patients with disability progression confirmed as 12 weeks in a time-to-event analysis that defined disability progression as an increase in the Expanded Disability Status Scale (EDSS) of at least 1.0 point from baseline that was sustained on subsequent visits for at least 12 weeks if the baseline score was 5.5 or less or an increase of at least
0.5 points that was sustained for at least 12 weeks if the baseline EDSS score was more than 5.5.

The percentage of patients with primary progressive MS with 12-week confirmed disability progression was 32.9% with Ocrevus vs. 39.3% with placebo (P = 0.03). The percentage of patients with 24-week confirmed disability progression was 29.6% with Ocrevus vs. 35.7% with placebo (P = 0.04). By Week 120, performance on the timed 25-foot walk worsened by 38.9% with Ocrevus vs. 55.1 % with placebo (P = 0.04). More favorable MRI results on several parameters were also observed with Ocrevus compared with placebo

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Ocrevus (ocrelizumab) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Other exclusions for coverage include, but are not limited to: Active hepatitis B or hepatitis C virus infection or another active infection at initiation of therapy; History of life- threatening infusion reaction to Ocrevus (ocrelizumab); Prescribed to treat any of the following conditions: secondary progressive multiple sclerosis, systemic lupus erythematosus; or rheumatoid arthritis; Use in combination with other immune-modulating or immunosuppressive therapies, including immunosuppressant doses of corticosteroids; Concurrent use with live vaccines or live attenuated vaccines

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J2350	Injection,ocrelizumab,1mg

AVAILABLE DOSAGE FORMS:
Ocrevus SOLN 300MG/10ML

REFERENCES

1. Ocrevus™ injection for intravenous infusion [prescribing information]. San Francisco, CA:Genentech, Inc; March 2021
2. Hauser SL, Bar-Or A, Comig G, et al, for the OPERA I and OPERA II Clinical Investigators. Ocrelizumab versus interferon beta-1a in relapsing multiple sclerosis. N Engl J Med. 2016 Dec
21. [Epub ahead of print].
3. Montalban X, Hauser SL, Kappos L, et al, for the ORATORIO Clinical Investigators. Ocrelizumab versus placebo in primary progressive multiple sclerosis. N Engl J Med. 2016 Dec 21. [Epub ahead of print].
4. Clinical bulletin. Information for health professionals. Overview of multiple sclerosis. RosalindKalb and Nancy Reitman. © 2012 National Multiple Sclerosis Society. Available at:
http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Brochures/Cli ni cal_Bulletin_Overview-ofMultiple-Sclerosis.pdf. Accessed on March 7, 2017.
5. Consensus Paper by the Multiple Sclerosis Coalition. The use of disease-modifying therapiesin multiple sclerosis: principles and current evidence. July 2014. Available at: Accessed on March 7, 2017.
6. Gajofatto A, Turatti M, Benedetti MD. Primary progressive multiple sclerosis: current therapeutic strategies and future perspectives. Expert Rev Neurother. 2016 Nov
15:1- 14.[Epub ahead of print]
7. 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 [published correction appears in Neurology. 2019;92(2):112]. Neurology. 2018;90(17):777-788. doi: 10.1212/WNL.0000000000005347. [PubMed 29686116]
8. Thompson, A., Banwell, B., et al. (2018). Diagnosis of multiple sclerosis: 2017 revisions of theMcDonald criteria. The Lancet Neurology, 17(2), pp.162-173

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Duration of Approval References	Q2 2022
Q2 2022 Established tracking in new format	Historical changes on file