Original Effective Date: 04/2021
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Last P&T Approval/Version: 04/30/2025
Next Review Due By: 04/2026
Policy Number: C21104-A

Kesimpta (ofatumumab)

PRODUCTS AFFECTED

Kesimpta (ofatumumab)

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 (MS)

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. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. RELAPSING FORMS OF MULTIPLE SCLEROSIS:
1. Documentation of a definitive diagnosis of a relapsing form of multiple sclerosis including: Relapsing-remitting multiple sclerosis [RRMS], secondary-progressive multiple sclerosis [SPMS] with relapses, and clinically isolated syndrome
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. (a) Documentation of **inadequate response (trial of 3 months) to ONE of the following: i) Interferon therapy (Avonex, Rebif, Extavia, Betaseron, Plegridy) OR ii) Glatiramer OR iii) formulary oral disease modifying therapy [e.g., Aubagio (teriflunomide), Tecfidera (dimethyl fumarate), Gilenya (fingolimod), etc.]
   **Inadequate response is defined as meeting at least TWO of the following three criteria during treatment: 1) Clinical relapses (at least two relapses within the past 12 months), 2) CNS lesion progression as measured by MRI, OR 3) Worsening disability (e.g., sustained worsening of EDSS score or neurological exam findings; worsening disability including, 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 $\geq$ 40 years of age, (ii) male gender, (iii) African American, (iv) motor, sphincter, brainstem-cerebellar symptoms, (v) MRI lesions in brainstem or spinal cord, OR (vi) $\geq$ 2 acute relapses in first 2 years of onset with significant sustained disability following relapse
   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 Kesimpta (ofatumumab) include: Active hepatitis B virus infection, History of hypersensitivity to ofatumumab or life-threatening injection-related reaction to Kesimpta.]
   AND
5. IF REQUEST IS FOR A NON-FORMULARY/NON-PREFERRED PRODUCT: Documentation of trial/failure of, or serious side effects to a majority (not more than 3) of the preferred formulary/PDL alternatives for the given diagnosis. Submit documentation including medication(s) tried, dates of trial(s) and reason for **treatment failure(s).
   **May be defined as meeting at least TWO of the following three criteria during treatment:
   1) Clinical relapses (at least two relapses within the past 12 months), 2) CNS lesion 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)

CONTINUATION OF THERAPY:

A. RELAPSING FORMS OF MULTIPLE SCLEROSIS:

1. Documentation of positive clinical response or stable disease based on ONE of the following:
   (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 the last 6 months) MRI shows lack of development of new asymptomatic lesions
   AND
2. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
3. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity (e.g., serious opportunistic or recurrent infections, etc.)

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. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests.]

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
Initial dosing: 20 mg by subcutaneous injection at Weeks 0, 1, and 2
Subsequent dosing: 20 mg by subcutaneous injection once monthly starting at Week 4

PLACE OF ADMINISTRATION:
The recommendation is that injectable medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Subcutaneous

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

COMPENDIAL APPROVED OFF-LABELED USES:
None

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:

Kesimpta, a CD20-directed cytolytic monoclonal antibody, is the first B-cell therapy that is intended for patient self-administration by subcutaneous injection. It is believed to work by binding to CD20, a cell surface antigen present on pre-B and mature B lymphocytes, thereby inducing B-cell lysis and depletion. The approval was based on efficacy and safety data from the phase 3 ASCLEPIOS I and II trials that compared ofatumumab with teriflunomide, a pyrimidine synthesis inhibitor, in 1882 adult patients with RMS. Findings from the studies showed ofatumumab significantly lowered the annualized relapse rate (primary end point) compared with teriflunomide. Additionally, ofatumumab significantly reduced the risk of3-month confirmed disability progression vs teriflunomide, as well as the number of T1 gadolinium-enhancing lesions and the rate of new or enlarging T2 lesions. As for safety, ofatumumab demonstrated a similar profile to teriflunomide with the most common adverse reactions being upper respiratory tract infection, headache, injection-related reactions, and local injection site reactions.

Progressive Multifocal Leukoencephalopathy

Progressive multifocal leukoencephalopathy (PML) is an opportunistic viral infection of the brain caused by the JC virus (JCV) that typically occurs in patients who are immunocompromised, and that usually leads to death or severe disability. Although no cases of PML have been reported for Kesimpta in the RMS clinical studies, PML resulting in death has occurred in patients being treated with ofatumumab for CLL (at substantially higher intravenous doses than the recommended dose in MS but for a shorter duration of treatment). In addition, JCV infection resulting in PML has also been observed in patients treated with other anti-CD20 antibodies and other MS therapies. At the first sign or symptom suggestive of PML, withhold Kesimpta and perform an appropriate diagnostic evaluation. Magnetic resonance

imaging (MRI) findings may be apparent before clinical signs or symptoms. Typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes. If PML is confirmed, treatment with Kesimpta should be discontinued. Arzerra (ofatumumab) for CLL is no longer commercially available and is obtained through a manufacturer access program.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:

All other uses of Kesimpta (ofatumumab) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Kesimpta (ofatumumab) include: active hepatitis B virus (HBV) infection, History of hypersensitivity to ofatumumab or life-threatening injection-related reaction to Kesimpta.

Exclusions/Discontinuation:

Based on animal data, Kesimpta can cause fetal harm. Advise females of reproductive potential to use effective contraception while receiving Kesimpta and for at least 6 months after the last dose.
Prior to initiating Kesimpta, perform testing for quantitative serum immunoglobulins. For patients with low serum immunoglobulins, consult immunology experts before initiating treatment with Kesimpta.
Monitor the levels of quantitative serum immunoglobulins during treatment, especially in patients with opportunistic or recurrent infections, and after discontinuation of therapy until B-cell repletion. Consider discontinuing Kesimpta therapy if a patient with low immunoglobulins develops a serious opportunistic infection or recurrent infections, or if prolonged hypogammaglobulinemia requires treatment with intravenous immunoglobulins.
Because vaccination with live-attenuated or live vaccines is not recommended during treatment and after discontinuation until B-cell repletion, administer all immunizations according to immunization guidelines at least 4 weeks prior to initiation of Kesimpta for live or live-attenuated vaccines and, whenever possible, at least 2 weeks prior to initiation of Kesimpta for non-live vaccines.
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).

OTHER SPECIAL CONSIDERATIONS:

None

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
N/A	

AVAILABLE DOSAGE FORMS:

REFERENCES

1. Kesimpta (ofatumumab) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals; April 2024.
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. Rosalind Kalb and Nancy Reitman. © 2012 National Multiple Sclerosis Society. Available at: Accessed on March 7, 2017.
5. Consensus Paper by the Multiple Sclerosis Coalition. The use of disease-modifying therapies in 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 the McDonald criteria. The Lancet Neurology, 17(2), pp.162-173

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Place of Administration Contraindications/Exclusions/Discontinuation References	Q2 2025
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Available Dosage Forms References	Q2 2024
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Quantity Background References	Q2 2023
REVISION- Notable revisions: Duration of Approval Prescriber Requirements Place of Administration References	Q2 2022
Q2 2022 Established tracking in new format	Historical changes on file