09-J3000-84

Original Effective Date: 04/01/21

Reviewed: 06/12/24

Revised: 07/15/24

Subject: Ofatumumab (Kesimpta)

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DESCRIPTION:

Multiple sclerosis (MS) is a chronic disease affecting the central nervous system (CNS). It is characterized by triad of inflammation, demyelination, and scarring of the central nervous system and manifests as pathological (immune-mediated CNS demyelination and axonal injury) and clinical (exacerbations, disability progression) dissemination in time and space. MS has been categorized into four types: clinically isolated syndrome (CIS), relapsing-remitting (RRMS), secondary progressive (SPMS), and primary progressive (PPMS). The most common type is RRMS, which is characterized by acute attacks followed by periods of remission. An initial attack may present as a clinically isolated syndrome (CIS); individuals presenting with this syndrome are high risk for subsequent conversion to clinically definite MS (CDMS) when coupled with MRI lesions consistent with MS. Although a cure for MS remains elusive, several treatment options slow the progression of the disease and reduce the frequency of relapses.

Ofatumumab is monoclonal antibody that is used to reduce the frequency of relapses and delay the accumulation of physical disability in patients with RRMS. It exerts its physiologic effects through binding to CD20 on the surface of B lymphocytes which results in complement-mediated cell lysis. Ofatumumab is Food and Drug administration (FDA) approved for the treatment of relapsing forms of MS to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

The efficacy of ofatumumab for the treatment of relapsing multiple sclerosis was compared to teriflunomide in two randomized, double-blind trials. Subjects were required to have at least one relapse in the prior year, 2 relapses in the previous 2 years, or the presence of a T1 gadolinium-enhancing lesion in the previous year. The subjects were also required to have an Expanded disability status scale score less than 5.5. The primary endpoint was the annualized relapse rate (ARR) over the treatment period. Approximately 60% of patients had previously received treatment with a non-steroid therapy for MS and a mean time since MS diagnosis of 5.6 years. In both trials, ofatumumab significantly

reduced annualized MS relapse rates compared to teriflunomide (Study 1, 0.11 vs 0.22, relative reduction = 51%;Study 2, 0.10 vs 0.25, RR=59%). The proportion of patients with 3-month confirmed disability progression was also reduced in the subjects treated with ofatumumab as compared to teriflunomide (10.9% vs 15%, relative risk reduction=34.4%). The mean number of T1 gadolinium-enhancing lesions per MRI and number of new or enlarging T2 lesions were also significantly reduced for subjects treated with ofatumumab as compared to teriflunomide. The most common adverse reactions that occurred were upper respiratory tract infection, headache, injection-related reactions, and local injection site reactions.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

NOTE: Avonex, Betaseron, Kesimpta, Mavenclad, Mayzent, Plegridy, Rebif, and Zeposia are the preferred brand products for treatment of relapsing forms of multiple sclerosis. The preferred generic products include dimethyl fumarate (generic), fingolimod (generic), glatiramer acetate (generic by Mylan), and teriflunomide (generic). Dimethyl fumarate (generic), fingolimod (generic), glatiramer acetate (generic by Mylan, Glatopa), and teriflunomide (generic) do not require prior authorization.

Initiation of ofatumumab (Kesimpta®) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. The member is diagnosed with **ONE** of the following forms of multiple sclerosis (MS):
    a. Relapsing remitting multiple sclerosis [RRMS]
    b. Active secondary progressive MS [SPMS]
    c. First clinical episode and member has MRI features consistent with MS
3. Ofatumumab will not be used in combination with **ANY** of the following:
    a. Alemtuzumab (Lemtrada)
    b. Cladribine (Mavenclad)
    c. Dimethyl fumarate (Tecfidera)
    d. Diroximel fumarate (Vumerity)
    e. Fingolimod (Gilenya, Tascenso ODT)
    f. Glatiramer acetate (Copaxone, Glatopa)
    g. Interferon beta-1a (Avonex, Rebif)
    h. Interferon beta-1b (Betaseron, Extavia)
    i. Mitoxantrone (Novantrone)

j. Monomethyl fumarate (Bafiertam)
k. Natalizumab (Tysabri)
l. Ocrelizumab (Ocrevus)
m. Ozanimod (Zeposia)
n. Peg-interferon beta-1a (Plegridy)
o. Ponesimod (Ponvory ODT)
p. Rituximab (Rituxan or biosimilars)
q. Siponimod (Mayzent)
r. Teriflunomide (Aubagio)
s. Ublituximab (Briumvi)

4. The member does not have an active Hepatitis B viral (HBV) infection
5. The initial dosage does not exceed 20 mg at week 0, 1, and 2, followed by 20 mg every 4 weeks starting at week 4

Approval duration: 1 year

Continuation of ofatumumab therapy **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member has demonstrated a beneficial response to therapy for treatment of RRMS, active SPMS, or clinically isolated syndrome
2. Authorization/reauthorization for ofatumumab has been previously approved by Florida Blue or another health plan in the past 2 years, **OR** the member previously met all indication-specific initiation criteria
3. Ofatumumab will not be in combination with **ANY** of the following:
    a. Alemtuzumab (Lemtrada)
    b. Cladribine (Mavenclad)
    c. Dimethyl fumarate (Tecfidera)
    d. Diroximel fumarate (Vumerity)
    e. Fingolimod (Gilenya, Tascenso ODT)
    f. Glatiramer acetate (Copaxone, Glatopa)
    g. Interferon beta-1a (Avonex, Rebif)
    h. Interferon beta-1b (Betaseron, Extavia)
    i. Mitoxantrone (Novantrone)
    j. Monomethyl fumarate (Bafiertam)
    k. Natalizumab (Tysabri)
    l. Ocrelizumab (Ocrevus)

m. Ozanimod (Zeposia)
n. Peg-interferon beta-1a (Plegridy)
o. Ponesimod (Ponvory)
p. Rituximab (Rituxan or biosimilars)
q. Siponimod (Mayzent)
r. Teriflunomide (Aubagio)
s. Ublituximab (Briumvi)

4. The dose does not exceed 20 mg every 4 weeks

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

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

- 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

Administer in the abdomen, thigh, or outer upper arm subcutaneously. Do not give injection into moles, scars, stretch marks or areas where the skin is tender, bruised, red, scaly, or hard.

Dose Adjustments

- Ofatumumab has not been studied in patients with renal or hepatic impairment

Drug Availability

20 mg/0.4 mL in a single-dose prefilled Sensoready Pen and single-dose prefilled syringe

PRECAUTIONS:

Boxed Warning

- none

Contraindications

- Active Hepatitis B Virus (HBV) infection

Precautions/Warnings

Infections: Delay administration in patients with an active infection until the infection is resolved. Vaccination with live-attenuated or live vaccines is not recommended during treatment and after discontinuation, until B-cell repletion.

Injection-Related Reactions: Management for injection-related reactions depends on the type and severity of the reaction.

Reduction in Immunoglobulins: Monitor the level of immunoglobulins at the beginning, during, and after discontinuation of treatment until B-cell repletion. Consider discontinuing if a patient develops a serious

opportunistic infection or recurrent infections if immunoglobulin levels indicate immune compromise.

Fetal Risk: May cause fetal harm based on animal data. Advise females of reproductive potential of the potential risk to a fetus and to use an effective method of contraception during treatment and for 6 months after stopping.

BILLING/CODING INFORMATION:

HCPCS Coding

J3590	Unclassified biologics

ICD-10 Diagnosis Codes That Support Medical Necessity

G35	Multiple sclerosis

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

Clinically isolated syndrome (CIS): the first clinical presentation of disease that shows characteristics of inflammatory demyelination that could be MS but has yet to fulfill criteria of dissemination in time.

Primary-progressive multiple sclerosis (PPMS): Steadily progressive course from onset; occurs in 10-15% of patients with MS.

Relapsing-remitting multiple sclerosis (RRMS): Characterized by acute attacks followed by periods of remission; primary form of MS that occurs in approximately 85% of patients.

Secondary-progressive multiple sclerosis (SPMS): An initial period of RRMS, followed by a steadily progressive course, with acute relapses (active disease) or without acute relapses (not active disease); 75-85% of patients diagnosed with RRMS will transition to SPMS.

RELATED GUIDELINES:

Alemtuzumab (Lemtrada), 09-J2000-27
Cladribine (Mavenclad), 09-J3000-34
Dimethyl Fumarate (Tecfidera), Diroximel fumarate (Vumerity), Monomethyl fumarate (Bafiertam), 09-J1000-96
Fingolimod (Gilenya), 09-J1000-30
Multiple Sclerosis Self Injectable Therapy, 09-J1000-39
Natalizumab (Tysabri) IV, 09-J0000-73
Ocrelizumab (Ocrevus), 09-J2000-78
Ozanimod (Zeposia), 09-J3000-70
Siponimod (Mayzent), 09-J3000-35
Teriflunomide (Aubagio), 09-J1000-82

OTHER:

None applicable

REFERENCES:

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3. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2023-09-29].
4. Hauser SL, Bar-Or A, Cohen JA et al. Ofatumumab versus teriflunomide in multiple sclerosis. N Engl J Med. 2020; 383: 546 – 557.
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7. Multiple Sclerosis Coalition. Available at http://www.nationalmssociety.org Accessed 10/30/20.
8. National Multiple Sclerosis Society. Accessed 10/30/20.
9. Rae-Grant A, Day GS, Marrie RA et al. Practice guideline: Disease-modifying therapies for adults with multiple sclerosis: Report of the guideline development, dissemination, and implementation

subcommittee of the American Academy of Neurology. April 2018. Available at: https://www.aan.com/Guidelines/home/GuidelineDetail/898.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 06/12/24

GUIDELINE UPDATE INFORMATION:

04/01/20	New Medical Coverage Guideline.
10/15/22	Review and revision to guideline; consisting of updating the list of agents not to be used in combination.
01/01/23	Review and revision to guideline; consisting of updating the position statement to include generic fingolimod as a preferred generic and removal of Gilenya as a preferred brand.
05/15/23	Revision to guideline; consisting of updating the position statement to include generic teriflunomide as a preferred generic and removal of Aubagio as a preferred brand. Updated list of agents not to be used in combination.
11/15/23	Review and revision to guideline; consisting of updating the position statement to include Glatopa.
07/15/24	Review and revision to guideline; consisting of updating the position statement to remove step requirement.