Multiple Sclerosis

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Multiple Sclerosis drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines and clinical studies while steering utilization to the most cost-effective medication within the therapeutic class. For this program, Bafiertam, Betaseron, Rebif, Copaxone 40mg, Glatopa 40mg, glatiramer acetate 40mg, Gilenya, generic dimethyl fumarate, Mayzent, Zeposia, and Aubagio are the preferred products. The criteria will require the use of the health plan’s preferred products for multiple sclerosis (Bafiertam, Betaseron, Rebif, Copaxone 40mg, Glatopa 40mg, glatiramer acetate 40mg, Gilenya, generic dimethyl fumarate, Mayzent, Zeposia, Aubagio) before the use of targeted product (Extavia, Vumerity, and brand Tecfidera) unless there are clinical circumstances that exclude the use of the preferred products. The program also considers Tysabri a preferred product. The criteria will require the use of the health plan’s preferred product for multiple sclerosis, Tysabri, before the use of the targeted product. Lemtrada. Avonex, Kesimpta, Ocrevus, Plegridy, and Mavenclad are excluded from the preferred multiple sclerosis product requirements.

POLICY

Must meet BOTH the Preferred Drug Plan Design (for the specific drug) and Criteria for Initial Approval/Continuation of Therapy when both are applicable.

<u>Preferred Drug Plan Design</u>

I. Criteria for initial approval for Extavia will only apply when the following criteria are met:

a. There is a documented clinical reason that the member must use Extavia over Betaseron. (Please note that Extavia and Betaseron are the exact same products with different labels and brand names, which are made in the same manufacturing facility.)
AND
b. Member has had a documented inadequate response or intolerable adverse effect with at least two of the preferred products other than Betaseron; **OR** Member is currently receiving therapy with Extavia, excluding when Extavia is obtained as samples or via manufacturer's patient assistance programs, and experiencing a positive therapeutic outcome

II. Criteria for initial approval for Vumerity will only apply when at least ONE of the following criteria are met:
a. Member has had a documented inadequate response or intolerable adverse effect to treatment with at least three of the preferred products
b. Member is currently receiving therapy with Vumerity, excluding when Vumerity is obtained as samples or via manufacturer's patient assistance programs, and experiencing a positive therapeutic outcome

III. Criteria for initial approval for Brand Tecfidera will only apply when at least ONE of the following criteria are met:
a. Member has had a documented inadequate response or intolerable adverse effect to treatment with at least three of the preferred products
b. Member is currently receiving therapy with brand Tecfidera, excluding when brand Tecfidera is obtained as samples or via manufacturer's patient assistance programs, and experiencing a positive therapeutic outcome

IV. Criteria for initial approval for Lemtrada will only apply when at least ONE of the following criteria are met:
a. Member is currently receiving treatment with Lemtrada, excluding when the Lemtrada is obtained as samples or via manufacturer's patient assistance programs, and experiencing a positive therapeutic outcome
b. Member has experienced a documented inadequate response and/or intolerable adverse event to treatment with Tysabri.
c. Member has a documented contraindication to therapy with Tysabri or any of its components.

<u>Criteria for Initial Approval</u>

I. **Aubagio** (teriflunomide), **Gilenya** (fingolimod), **Mayzent** (siponimod), brand and generic **Tecfidera** (dimethyl fumarate), **Vumerity** (diroximel fumarate), **Bafiertam** (monomethyl fumarate) and **Zeposia** (ozanimod) may be considered **medically necessary** for members who have been diagnosed with a relapsing form of multiple sclerosis (including clinically isolated syndrome, relapsing-remitting disease or active secondary progressive disease).

Approval will be for **12 months.**

II. **Avonex** (interferon beta-1α), **Betaseron** (interferon beta-1β), and **Rebif** (interferon beta-1α) may be considered **medically necessary** for members who have been diagnosed with a relapsing form of multiple sclerosis (including clinically isolated syndrome, relapsing-remitting disease or active secondary progressive disease).

Approval will be for **12 months.**

III. **Brand and generic Copaxone 40mg** (glatiramer acetate) and **Glatopa 40mg** (glatiramer acetate) may be considered **medically necessary** for members who have been diagnosed with a relapsing form of multiple sclerosis (including clinically isolated syndrome, relapsing-remitting disease or active secondary progressive disease).

Approval will be for **12 months.**

IV. **Extavia** (interferon beta-1β) may be considered **medically necessary** when ALL of the following criteria are met:
   a. Member must have been diagnosed with a relapsing form of multiple sclerosis (including clinically isolated syndrome, relapsing-remitting disease or active secondary progressive disease).

Approval will be for **12 months.**

V. **Plegridy** (peginterferon beta-1α) may be considered **medically necessary** for members who have been diagnosed with a relapsing form of multiple sclerosis (including clinically isolated syndrome, relapsing-remitting disease or active secondary progressive disease).

Approval will be for **12 months.**

VI. **Ocrevus** (ocrelizumab) may be considered **medically necessary** for the treatment of relapsing forms of multiple sclerosis (including clinically isolated syndrome, relapsing-remitting disease or active secondary progressive disease).

Approval will be for **12 months.**

VII. **Ocrevus** (ocrelizumab) may be considered **medically necessary** for the treatment of primary progressive multiple sclerosis.

Approval will be for **12 months.**

VIII. The first course of **Lemtrada** (alemtuzumab) may be considered **medically necessary** for the treatment of relapsing forms of MS when the following criteria is met:
   a. The member has had an inadequate response to two or more drugs indicated for multiple sclerosis;

   AND

   b. The member must meet one of the following exclusion criteria:
      - Member is currently receiving treatment with Lemtrada, excluding when the Lemtrada is obtained as samples or via manufacturer's patient assistance programs.
      - Member has experienced a documented inadequate response and/or intolerable adverse event to treatment with Tysabri.
      - Member has a documented contraindication to therapy with Tysabri or any of its components.

Approval will be for **30 days (5 doses).**

IX. **Tysabri** (natalizumab) may be considered **medically necessary** as monotherapy for the treatment of a relapsing form of MS (e.g. relapsing-remitting multiple sclerosis and secondary progressive disease with relapses) when the following criteria is met:
   a. The member has tried and failed two multiple sclerosis therapies. Previous trial of another multiple sclerosis therapy is not required if the patient has evidence of highly active disease despite glatiramer or interferon-β as demonstrated by 1 relapse in the previous year and either a) at least one gadolinium-enhancing MRI lesion or (b) at least nine T2-hyperintensive lesions on cranial MRI

Approval will be for **12 months.**

X. **Tysabri** (natalizumab) may be considered **medically necessary** for the treatment of clinically isolated syndrome of multiple sclerosis.

Approval will be for **12 months.**

*****Tysabri (natalizumab) is also considered medically necessary for the treatment of moderate to severe Crohn's Disease (CD) refractory to other agents. Approval will be for lifetime.

XI. **Mavenclad** (cladribine) may be considered **medically necessary** for the treatment of relapsing forms of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapses) when all of the following criteria are met:
   a. Member has had an inadequate response, intolerable adverse event, or documented contraindication to ALL of the following:
      - At least one interferon therapy (e.g. Avonex, Betaseron, Plegridy, Rebif)
      - Copaxone, glatiramer acetate, or Glatopa
      - At least two oral therapies indicated for relapsing forms of MS (e.g. Aubagio, Gilenya, Tecfidera, Mayzent)
   b. Member does not have clinically isolated syndrome (CIS).
   c. Member has obtained a recent complete blood count (CBC) and lymphocytes are within normal limits
   d. Member has been screened for tuberculosis and hepatitis B and C
   e. Member has not received 2 courses (i.e., 4 cycles) of Mavenclad.
   f. Members will not use Mavenclad concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra and Nuedexta.

Approval will be for **45 days**.

XII. **Kesimpta** (ofatumumab) may be considered **medically necessary** when BOTH of the following criteria are met:
   a. Member has been diagnosed with a relapsing form of multiple sclerosis (including clinically isolated syndrome, relapsing-remitting disease or active secondary progressive disease).
   b. The member must meet one of the following exclusion criteria:
      a. Member is currently receiving treatment with Kesimpta, excluding when Kesimpta is obtained as samples or via manufacturer's patient assistance programs.
      b. Member has experienced a documented inadequate response and/or intolerable adverse event to treatment with Ocrevus.
      c. Member has a documented contraindication to therapy with Ocrevus or any of its components.

Approval will be for **12 months**.

Continuation of Therapy

I. The continuation of **Aubagio** (teriflunomide), **Avonex** (interferon beta-1α), **Betaseron** (interferon beta-1β), **Copaxone 40mg** (glatiramer acetate), **Extavia** (interferon beta-1β), **Glatopa 40mg** (glatiramer acetate), **Gilenya** (fingolimod), Kesimpta (ofatumumab), **Mayzent** (siponimod), **Ocrevus** (ocrelizumab), **Plegridy** (peginterferon beta-1α), **Rebif** (interferon beta-1α), brand and generic **Tecfidera** (dimethyl fumarate), **Tysabri** (natalizumab), **Vumerity** (diroximel fumarate), **Bafiertam** (monomethyl fumarate), and **Zeposia** (ozanimod) may be considered **medically necessary** for members who meet initial criteria for approval above and are experiencing disease stability or improvement while receiving the requested medication.

Approval will be for **12 months.**

II. Subsequent courses of **Lemtrada** (alemtuzumab) may be considered **medically necessary** for the treatment of relapsing forms of MS when the member meets all of the following criteria:
   a. The member has completed at least one previous course of therapy
   b. The member must have received the previous course of Lemtrada treatment at least 12 months prior to the planned date of the first dose of Lemtrada course of treatment.

Approval will be for **30 days (3 doses).**

III. The continuation of **Mavenclad** (cladribine) may be considered **medically necessary** for the treatment of relapsing forms of MS (including relapsing-remitting and secondary progressive disease for those who continue to experience relapses) when the member meets all of the following criteria:
   a. Member has had an inadequate response or is unable to tolerate ALL alternative drugs indicated for the treatment of relapsing forms of multiple sclerosis.
   b. Member has not received 2 courses (i.e., 4 cycles) of Mavenclad.
   c. Member has obtained a complete blood count (CBC) with differential including lymphocyte count and lymphocytes are at least 800 cells/uL
   d. The member has not received Mavenclad in the last 43 weeks.

   Approval will be for **45 days.**

The aforementioned drugs are considered **not medically necessary** for patients who do not meet the criteria set forth above.

Other Criteria

Members will not use the requested medication concomitantly with other medications used for the treatment of multiple sclerosis, excluding Ampyra and Nuedexta, because there is inadequate evidence that use of two or more these drugs in combination results in better clinical outcomes than use of a single drug.

Dosage and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limits

Trade Name	Generic Name	Quantity Limit
Aubagio®	teriflunomide	30 tablets per 30 days
Avonex®	interferon beta-1α	4 vials per 28 days
Betaseron®	interferon beta-1β	15 vials per 30 days
Copaxone® 40 mg Glatopa 40mg	glatiramer acetate	12 syringes per 28 days
Extavia®	interferon beta-1β	15 vials per 30 days
Gilenya™	fingolimod	30 capsules per 30 days
Kesimpta	ofatumumab	Initiation of therapy: 4 pens per 28 days Maintenance: 1 pen per 28 days
Mavenclad	cladribine	20 tablets per 9 months
Mayzent	siponimod	Initiation of therapy: 1 starter pack (12 tablets) per first 5 days Maintenance: 1-2mg per day
Ocrevus	ocrelizumab	Initiation of therapy: 300 mg infusion on day 1 and 15 Maintenance: 600 mg every 6 months
Plegridy™	peginterferon beta-1α	Initiation of therapy: 1 starter pack per first 28 days Maintenance: 2 pens per 28 days
Rebif®	interferon beta-1α	12 vials per 28 days
Tecfidera™	dimethyl fumarate	Initiation of therapy: 1 starter pack per first 28 days Maintenance: 60 capsules per 30 days
Tysabri®	natalizumab	1 vial per 28 days
Vumerity	diroximel fumarate	Initiation of therapy: 1 starter dose bottle (106 capsules) per first 28 days Maintenance: 120 capsules per 28 days
Zeposia	ozanimod	Initiation of therapy: 1 starter pack (4- 0.23 mg capsules and 3- 0.46 mg capsules) per first 7 days or 1 starter kit (4- 0.23 mg capsules, 3- 0.46 mg capsules, and 30- 0.92 mg capsules) per first 37 days Maintenance: 30- 0.92 mg capsules per 30 days
Bafiertam	monomethyl fumarate	120 capsules per 30 days

CLINICAL RATIONALE FOR KESIMPTA

Multiple Sclerosis (MS) is a chronic, inflammatory, autoimmune disease of the central nervous system that disrupts communications within the brain and between the brain and body. MS often starts with a relapsing-

remitting course, in which episodes of worsening function (relapses) are followed by recovery periods (remissions) that may not be complete and may leave patients with some degree of residual disability. Many patients with MS experience some degree of persistent disability that gradually worsens over time. Some patients experience secondary progressive multiple sclerosis (SPMS), where disability progresses independently of relapses. In the first few years of this process, many patients continue to experience a relapsing form of MS known as active SPMS. Drugs approved for the treatment of relapsing forms of MS can be used to treat active SPMS. Up to 80% of patients with relapsing-remitting MS (RRMS), the most common form of MS at diagnosis, will develop SPMS. SPMS is a form of MS characterized by progressive and irreversible disability. Most patients transition from RRMS to SPMS over many years, which can vary if a patient is receiving an MS disease-modifying drug treatment or not.

On August 20, 2020, Genmab and Novartis announced the FDA approval of Kesimpta (ofatumumab), 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. The precise mechanism by which Kesimpta exerts its therapeutic effects in MS is unknown, but is presumed to involve binding to CD20, a cell surface antigen present on pre-B and mature B cells (lymphocytes). Following cell surface binding to B cells (lymphocytes), Kesimpta results in antibody-dependent cellular cytolysis and complement-mediated lysis.

Kesimpta has shown superior efficacy and a similar safety profile compared with Aubagio. It is in the same class as ocrelizumab (Ocrevus) which is administered as an intravenous infusion every 6 months and demonstrates similar efficacy and safety when compared indirectly. Ofatumumab is also available as an intravenous formulation (Arzerra) indicated for chronic lymphocytic leukemia. Kesimpta is the first B-cell therapy that can be self-administered monthly via subcutaneous injection at home.

The efficacy of Kesimpta was established in two double-blind, active comparator studies in 1,882 patients with relapsing forms of MS. Patients were randomized to Kesimpta or teriflunomide. The primary endpoint of both studies was the annualized relapse rate (ARR) over the treatment period. In study 1, the ARR was 0.11 for the Kesimpta group vs. 0.22 for the teriflunomide group (Relative reduction: 51%; $p < 0.001$). In study 2, the ARR was 0.10 for the Kesimpta group vs. 0.25 for the teriflunomide group (Relative reduction: 59%; $p < 0.001$). Kesimpta demonstrated a significant reduction in active MRI-detected lesions (a relative reduction of 94 to 98%), new or enlarging lesions (a relative reduction of 82 to 85%), and disability progression sustained over 3 months (a relative reduction of 34.4%). Brain tissue loss was not reduced significantly more in the Kesimpta group.

Kesimpta is contraindicated in patients with active hepatitis B virus infection. Warnings and precautions for Kesimpta include infections, injection-related reactions, reduction in immunoglobulins, and fetal risk. The most common adverse reactions (> 10%) with Kesimpta use were upper respiratory tract infection, headache, injection-related reactions, and local injection site reactions.

The recommended dose of Kesimpta is initial dosing of 20 mg by subcutaneous (SC) injection at weeks 0, 1, and 2, followed by subsequent dosing of 20 mg by SC injection once monthly starting at week 4. Kesimpta is intended for patient self-administration by SC injection.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD-CM diagnostic codes.

- J0202 - Injection, alemtuzumab, 1 mg
- J2323 - natalizumab, 1 mg
- J2350 – Injection, ocrelizumab (Ocrevus), 1mg

REFERENCES

- Aubagio [package insert].Cambridge, MA: Genzyme Corporation; September 2019.
- Avonex [package insert]. Cambridge, MA: Biogen Idec Inc.; July 2019.
- Betaseron [package insert]. Montville, NJ: Bayer HealthCare Pharmaceuticals Inc.; August 2019.
- Copaxone [package insert]. Kansas City, MO: Teva Neuroscience, Inc.; July 2019.
- Glatopa [package insert]. Princeton, NJ: Sandoz Inc.; October 2018.
- Glatiramer acetate [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; November 2018.
- Extavia [package insert]. East Hanover, NJ: Novartis Pharmaceutical Corporation; August 2019.
- Gilenya [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2019.
- Kesimpta [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2020.
- Lemtrada [package insert]. Cambridge, MA: Genzyme Corporation; January 2019.
- Mavenclad [package insert]. Rockland, MA; EMD Serono, Inc; April 2019.
- Mayzent [package insert]. East Hanover, NJ; Novartis Pharmaceuticals Corp; March 2019.
- Plegridy [package insert]. Cambridge, MA: Biogen Idec Inc.; July 2019.
- Rebif [package insert]. Rockland, MA; EMD Serono Inc.; July 2019.
- Tecfidera [package insert]. Cambridge, MA : Biogen Idec Inc.: July 2019.
- Tysabri [package insert]. Cambridge, MA: Biogen Idec Inc.; August 2019.
- Vumerity [package insert]. Cambridge, MA: Biogen; October 2019.
- The Multiple Sclerosis Coalition. *The use of disease-modifying therapies in multiple sclerosis: principles and current evidence.* http://www.nationalmssociety.org/getmedia/5ca284d3-fc7c-4ba5-b005-ab537d495c3c/DMT_Consensus_MS_Coalition_color. Accessed October 01, 2019.
- Ocrevus [package insert]. South San Francisco, CA: Genentech, Inc.; July 2019.
- Bafiertam [package insert]. High Point, NC: Banner Life Sciences LLC; April 2020.
- Zeposia [package insert]. Summit, NJ: Celgene Corporation; March 2020

*Some content reprinted from CVSHealth

POLICY HISTORY

Policy #: 05.01.75
Policy Creation: August 2008
Reviewed: October 2020
Revised: October 2020
Current Effective Date: January 15, 2021