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, Aubagio, Betaseron, Copaxone, generic dimethyl fumarate, generic fingolimod, Gilenya, glatiramer acetate, Glatopa, Mayzent, Ponvory, Rebif, Vumerity, and Zeposia are the preferred products. The criteria will require the use of the health plan's preferred products for multiple sclerosis (Aubagio, Betaseron, Copaxone, generic dimethyl fumarate, generic fingolimod, Gilenya, glatiramer acetate, Glatopa, Mayzent, Ponvory, Rebif, Vumerity, and Zeposia) before the use of targeted product (Bafiertam, Extavia, Tascenso ODT (fingolimod), and brand Tecfidera) unless there are clinical circumstances that exclude the use of the preferred products. The program also considers Ocrevus and Tysabri preferred products. The criteria will require the use of the health plan's preferred products for multiple sclerosis, Ocrevus, and Tysabri, before the use of the targeted product, Lemtrada. Avonex, Kesimpta, Mavenclad, and Plegridy, 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.

Preferred Drug Plan Design

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 **Bafiertam** 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 Bafiertam, excluding when Bafiertam is obtained as samples or via manufacturer's patient assistance programs, and experiencing a positive therapeutic outcome

III. Criteria for initial approval for **Tascenso ODT** 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 Tascenso ODT, excluding when Tascenso ODT is obtained as samples or via manufacturer's patient assistance programs, and experiencing a positive therapeutic outcome

IV. 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

V. Criteria for initial approval for the treatment of moderately to severely active ulcerative colitis with **Zeposia** will only apply when at least ONE of the following criteria are met:
a) Member has had an inadequate response to treatment or intolerable adverse event with at least TWO of the preferred products (Humira, Rinvoq, Stelara and Xeljanz/Xeljanz XR)
b. Member is currently receiving therapy with Zeposia, excluding when Zeposia is obtained as samples or via manufacturer's patient assistance programs, and experiencing a positive therapeutic outcome

VI. 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 both Ocrevus, AND Tysabri.
c. Member has a documented contraindication to therapy with both Ocrevus, AND Tysabri or any of their components.

Criteria for Initial Approval

I. **Aubagio** (teriflunomide), **Avonex** (interferon beta-1α), **Bafiertam** (monomethyl fumarate), **Betaseron** (interferon beta-1β), brand and generic **Copaxone** (glatiramer acetate), **Extavia** (interferon beta-1β), brand and generic **Gilenya** (fingolimod), **Glatopa** (glatiramer acetate), **Mayzent** (siponimod), **Plegridy** (peginterferon beta-1α), **Ponvory** (ponesimod), **Rebif** (interferon beta-1α), **Tascenco ODT** (fingolimod), brand and generic **Tecfidera** (dimethyl fumarate), **Vumerity** (diroximel fumarate), and **Zeposia** (ozanimod) may be considered **medically necessary** for members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

Approval will be for **12 months.**

II. **Aubagio** (teriflunomide), **Avonex** (interferon beta-1α), **Bafiertam** (monomethyl fumarate), **Betaseron** (interferon beta-1β), brand and generic **Copaxone** (glatiramer acetate), **Extavia** (interferon beta-1β), brand and generic **Gilenya** (fingolimod), **Glatopa** (glatiramer acetate), **Mayzent** (siponimod), **Plegridy** (peginterferon beta-1α), **Ponvory** (ponesimod), **Rebif** (interferon beta-1α), **Tascenso ODT** (fingolimod), brand and generic **Tecfidera** (dimethyl fumarate), **Vumerity** (diroximel fumarate), and **Zeposia** (ozanimod) may be considered **medically necessary** for the treatment of clinically isolated syndrome of multiple sclerosis.

Approval will be for **12 months.**

III. **Zeposia** (ozanimod) may be considered **medically necessary** for the treatment of moderately to severely active ulcerative colitis when BOTH of the following criteria are met:
   a. The member meets ONE of the following:
      i. Member has previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Xeljanz) indicated for the treatment of moderately to severely active ulcerative colitis.
      ii. Member has had an inadequate response, intolerance or contraindication to at least one conventional therapy option (see Appendix A).
   b. Zeposia will not be used concomitantly with immunomodulators, biologic therapy, or targeted synthetic drugs.

Approval will be for **12 months.**

Note: submission of chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy is necessary to initiate the prior authorization review. If therapy is not advisable, documentation of clinical reason to avoid therapy is necessary.

IV. **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 to or is unable to tolerate an alternative drug indicated for the treatment of multiple sclerosis
   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**.

V. **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:
      i. Member is currently receiving treatment with Kesimpta, excluding when Kesimpta is obtained as samples or via manufacturer's patient assistance programs and has achieved or maintained a positive clinical response as evidenced by experiencing disease stability or improvement.
      ii. Member has experienced a documented inadequate response and/or intolerable adverse event to treatment with Ocrevus.
      iii. Member has a documented contraindication to therapy with Ocrevus or any of its components.

Approval will be for **12 months**.

VI. **Ocrevus** (ocrelizumab) may be considered **medically necessary** for members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse).

Approval will be for **12 months.**

VII. **Ocrevus** (ocrelizumab) may be considered **medically necessary** for the treatment of clinically isolated syndrome of multiple sclerosis.

Approval will be for **12 months.**

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

Approval will be for **12 months.**

IX. 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

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

X. **Tysabri** (natalizumab) may be considered **medically necessary** for the treatment of moderately to severely active Crohn's disease (CD) in members who have received any other biologic indicated for the treatment of moderately to severely active Crohn's disease and who have been tested for anti-JCV antibodies.

Note: submission of chart notes, medical record documentation, or claims history supporting previous medications tried is necessary to initiate the prior authorization review.

Approval will be for **12 months.**

XI. **Tysabri** (natalizumab) may be considered **medically necessary** for members who have been diagnosed with a relapsing form of MS (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse) and those who have been tested for anti-JCV antibodies.

Approval will be for **12 months.**

XII. **Tysabri** (natalizumab) may be considered **medically necessary** for the treatment of clinically isolated syndrome and those who have been tested for anti-JCV antibodies.

Approval will be for **12 months.**

Continuation of Therapy

I. The continuation of **Aubagio** (teriflunomide), **Avonex** (interferon beta-1α), **Bafiertam** (monomethyl fumarate), **Betaseron** (interferon beta-1β), brand and generic **Copaxone** (glatiramer acetate), **Extavia** (interferon beta-1β), brand and generic **Gilenya** (fingolimod), **Glatopa** (glatiramer acetate), **Kesimpta** (ofatumumab), **Mayzent** (siponimod), **Ocrevus** (ocrelizumab), **Plegridy** (peginterferon beta-1α), **Ponvory** (ponesimod), **Rebif** (interferon beta-1α), **Tascenso ODT** (fingolimod), brand and generic **Tecfidera** (dimethyl fumarate), **Vumerity** (diroximel 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. The continuation of **Zeposia** (ozanimod) may be considered **medically necessary** for members who are using the requested medication for the treatment of moderately to severely active ulcerative colitis when BOTH of the following are met:
    a. The member has achieved or maintained remission.
    b. The member has achieved or maintained a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
        i. Stool frequency
        ii. Rectal bleeding
        iii. Urgency of defecation
        iv. C-reactive protein (CRP)
        v. Fecal calprotectin (FC)
        vi. Endoscopic appearance of the mucosa
        vii. Improvement on a disease activity scoring tool (e.g., Ulcerative Colitis Endoscopic Index of Severity [UCEIS], Mayo score)
    c. Zeposia will not be used concomitantly with immunomodulators, biologic therapy, or targeted synthetic drugs.

Approval will be for **12 months.**

Note: submission of chart notes or medical record documentation supporting positive clinical response to therapy or remission.

III. The continuation of **Mavenclad** (cladribine) may be considered **medically necessary** for members who meet initial criteria for approval above and meet ALL of the following:
   a. Member has not received 2 courses (i.e., 4 cycles) of Mavenclad.
   b. Member has obtained a complete blood count (CBC) with differential including lymphocyte count and lymphocytes are at least 800 cells/µL
   c. The member has not received Mavenclad in the last 43 weeks.

Approval will be for **45 days.**

IV. Subsequent courses of **Lemtrada** (alemtuzumab) may be considered **medically necessary** for the treatment of relapsing forms of multiple sclerosis 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).**

V. The continuation of **Tysabri** (natalizumab) may be considered **medically necessary** when member meets any of the following:
   a. Member is using the requested medication for moderately to severely active Crohn's disease and has achieved or maintained remission

      Note: submission of chart notes or medical record documentation supporting positive clinical response to therapy or remission.

   b. Member is using the requested medication for moderately to severely active Crohn's disease and has achieved or maintained a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:
      i. Abdominal pain or tenderness
      ii. Diarrhea
      iii. Body weight
      iv. Abdominal mass
      v. Hematocrit
      vi. Endoscopic appearance of the mucosa
      vii. Improvement on a disease activity scoring tool (e.g., Crohn's Disease Activity Index [CDAI] score)

      Note: submission of chart notes or medical record documentation supporting positive clinical response to therapy or remission.

   c. Member is using the requested medication for the treatment of relapsing forms of multiple sclerosis or clinically isolated syndrome of multiple sclerosis and has achieved or maintained a positive clinical response with the requested drug as evidenced by experiencing disease stability or improvement.

Approval will be for **12 months.**

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 disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying).

For **Tysabri**, members will not use the requested medication concomitantly with any other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying), immunosuppressants, or TNF inhibitors (e.g., adalimumab, infliximab).

Appendix A

1. Mild to moderate disease – induction of remission:
    a. Oral mesalamine (e.g., Asacol, Asacol HD, Lialda, Pentasa), balsalazide, olsalazine
    b. Rectal mesalamine (e.g., Canasa, Rowasa)
    c. Rectal hydrocortisone (e.g., Colocort, Cortifoam)
    d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine
2. Mild to moderate disease – maintenance of remission:
    a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine
    b. Alternatives: azathioprine, mercaptopurine, sulfasalazine
3. Severe disease – induction of remission:
    a. Prednisone, hydrocortisone IV, methylprednisolone IV
    b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine
4. Severe disease – maintenance of remission:
    a. Azathioprine, mercaptopurine
    b. Alternative: sulfasalazine

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, syringes, or pens per 28 days
Betaseron	interferon beta-1β	14 vials/syringes per 28 days
Bafiertam	monomethyl fumarate	120 capsules per 30 days
Copaxone 40mg Glatopa 40mg	glatiramer acetate	12 syringes per 28 days
Copaxone 20 mg Glatopa 20 mg	glatiramer acetate	30 syringes per 30 days

Trade Name	Generic Name	Quantity Limit
Extavia	interferon beta-1β	15 vials/syringes per 30 days
Gilenya	fingolimod	30 capsules per 30 days
Kesimpta	ofatumumab	Initiation of therapy: 3 pens per 15 days Maintenance: 1 pen per 28 days
Mavenclad	cladribine	20 tablets per 9 months
Mayzent	siponimod	Initiation of therapy: 1 starter pack per first 4-5 days Maintenance 0.25mg: 120 tablets per 30 days Maintenance 1mg or 2mg: 30 tablets per 30 days
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
Ponvory	Ponesimod	Initiation of therapy: 1 starter pack per first 14 days Maintenance: 30 tablets per 30 days
Rebif	interferon beta-1α	12 prefilled syringes or autoinjectors per 28 days
Tascenso ODT	fingolimod	30 orally disintegrating tablets per 30 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

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

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POLICY HISTORY

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