Medical Benefit Drug Policy

Multiple Sclerosis Agents (Lemtrada®, Ocrevus®, Ocrevus Zunovo™, Briumvi™)

Policy Number: MC/PC 025
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Instructions for Use

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Coverage Rationale

Primary Progressive Multiple Sclerosis (PPMS)

For initial coverage of Ocrevus (ocrelizumab) and Ocrevus Zunovo (ocrelizumab and hyaluronidase-ocsq for Primary Progressive Multiple Sclerosis (PPMS), the following will be required:

- Diagnosis of Primary Progressive Multiple Sclerosis (PPMS) **and**
- Not used in combination with another disease-modifying therapy for MS **and**
- Not used in combination with another B-cell targeted therapy (e.g., rituximab [Rituxan], belimumab [Benlysta], ofatumumab [Arzerra, Kesimpta]) **and**
- Not used in combination with another lymphocyte trafficking blocker (e.g., alemtuzumab [Lemtrada], mitoxantrone) **and**
- Prescribed by or in consultation with a neurologist.

For reauthorization coverage of Ocrevus (ocrelizumab) and Ocrevus Zunovo (ocrelizumab and hyaluronidase-ocsq for Primary Progressive Multiple Sclerosis (PPMS), the following will be required:

- Presence of positive clinical response to therapy (e.g., stability in radiologic disease activity, clinical relapses, disease progression) **and**
- Not used in combination with another disease-modifying therapy for MS **and**
- Not used in combination with another B-cell targeted therapy (e.g., rituximab [Rituxan], belimumab [Benlysta], ofatumumab [Arzerra, Kesimpta]) **and**
- Not used in combination with another lymphocyte trafficking blocker (e.g., alemtuzumab [Lemtrada], mitoxantrone) **and**
- Prescribed by or in consultation with a neurologist.

Relapsing Forms of Multiple Sclerosis (MS)

For initial coverage of Lemtrada (alemtuzumab) for Relapsing Forms of MS, the following will be required:

- All of the following:
  - Diagnosis of a relapsing form of multiple sclerosis (MS) (e.g., relapsing-remitting disease, secondary progressive disease, including active disease with new brain lesions) **and**
  - Patient has not been previously treated with alemtuzumab **and**
  - Not used in combination with another disease-modifying therapy for MS **and**
  - Prescribed by or in consultation with a neurologist.

OR

- All of the following:
  - Patient has previously received treatment with alemtuzumab **and**
  - At least 12 months have or will have elapsed since the most recent treatment course with alemtuzumab **and**
  - Not used in combination with another disease-modifying therapy for MS **and**
  - Prescribed by or in consultation with a neurologist.

For initial coverage of Briumvi (ublituximab-xiiy) for Relapsing Forms of MS, the following will be required:

- All of the following:
  - Diagnosis of a relapsing form of multiple sclerosis (MS) (e.g., clinically isolated syndrome, relapsing-remitting disease, secondary progressive disease, including active disease with new brain lesions) **and**
  - Not used in combination with another disease-modifying therapy for MS **and**
  - Not used in combination with another B-cell targeted therapy (e.g., rituximab [Rituxan], belimumab [Benlysta], ofatumumab [Arzerra, Kesimpta]) **and**
  - Not used in combination with another lymphocyte trafficking blocker (e.g., alemtuzumab [Lemtrada], mitoxantrone) **and**
  - Prescribed by or in consultation with a neurologist.

OR

- For continuation of prior therapy

For reauthorization coverage of Briumvi (ublituximab-xiiy) for Relapsing Forms of MS, the following will be required:

- Presence of positive clinical response to therapy (e.g., stability in radiologic disease activity, clinical relapses, disease progression) **and**
- Not used in combination with another disease-modifying therapy for MS **and**
- Not used in combination with another B-cell targeted therapy (e.g., rituximab [Rituxan], belimumab [Benlysta], ofatumumab [Arzerra, Kesimpta]) **and**
- Not used in combination with another lymphocyte trafficking blocker (e.g., alemtuzumab [Lemtrada], mitoxantrone) **and**
- Prescribed by or in consultation with a neurologist.

For initial coverage of Ocrevus (ocrelizumab) and Ocrevus Zunovo (ocrelizumab and hyaluronidase-ocsq) for Relapsing Forms of MS, the following will be required:

- All of the following:
  - Diagnosis of a relapsing form of multiple sclerosis (MS) (e.g., clinically isolated syndrome, relapsing-remitting disease, secondary progressive disease, including active disease with new brain lesions) **and**
  - Not used in combination with another disease-modifying therapy for MS **and**
  - Not used in combination with another B-cell targeted therapy (e.g., rituximab [Rituxan], belimumab [Benlysta], ofatumumab [Arzerra, Kesimpta]) **and**
  - Not used in combination with another lymphocyte trafficking blocker (e.g., alemtuzumab [Lemtrada], mitoxantrone) **and**
  - Prescribed by or in consultation with a neurologist.

OR

- All of the following:
  - For continuation of prior therapy **and**
  - Not used in combination with another disease-modifying therapy for MS **and**
  - Not used in combination with another B-cell targeted therapy (e.g., rituximab [Rituxan], belimumab [Benlysta], ofatumumab [Arzerra, Kesimpta]) **and**
  - Not used in combination with another lymphocyte trafficking blocker (e.g., alemtuzumab [Lemtrada], mitoxantrone) **and**
  - Prescribed by or in consultation with a neurologist.

For reauthorization coverage of Ocrevus (ocrelizumab) and Ocrevus Zunovo (ocrelizumab and hyaluronidase-ocsq for Relapsing Forms of MS, the following will be required:

- Documentation of positive clinical response to therapy (e.g., stability in radiologic disease activity, clinical relapses, disease progression) **and**
- Not used in combination with another disease-modifying therapy for MS **and**
- Not used in combination with another B-cell targeted therapy (e.g., rituximab [Rituxan], belimumab [Benlysta], ofatumumab [Arzerra, Kesimpta]) **and**
- Not used in combination with another lymphocyte trafficking blocker (e.g., alemtuzumab [Lemtrada], mitoxantrone) **and**
- Prescribed by or in consultation with a neurologist.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J0202	Injection, alemtuzumab, 1 mg
J2350	Injection, ocrelizumab, 1 mg
J2329	Injection, ublituximab-xiiy, 1 mg
J2351	Injection, ocrelizumab, 1 mg and hyaluronidase-ocsq

ICD-10 Code	Description
G35	Multiple sclerosis
G35.A	Relapsing-remitting multiple sclerosis
G35.B0	Primary progressive multiple sclerosis, unspecified
G35.B1	Active primary progressive multiple sclerosis
G35.B2	Non-active primary progressive multiple sclerosis
G35.C0	Secondary progressive multiple sclerosis, unspecified
G35.C1	Active secondary progressive multiple sclerosis
G35.C2	Non-active secondary progressive multiple sclerosis
G35.D	Multiple sclerosis, unspecified

Background

Multiple Sclerosis (MS), a chronic, immune-mediated disease of the central nervous system (CNS), is among the most common causes of neurological disability in young adults (Olek and Howard 2026[a]). MS is characterized by inflammation, demyelination, and degenerative changes in the CNS. Most patients with MS experience relapses and remissions of neurological symptoms, usually early in the disease process, with clinical events that are generally associated with CNS inflammation. There are 4 clinical subtypes of MS:

- Relapsing-remitting MS (RRMS), which is characterized by acute attacks followed by partial or full recovery. This is the most common form of MS, accounting for an estimated 85% to 90% of cases.
- Secondary progressive MS (SPMS) begins as RRMS, followed by gradual worsening, which may be accompanied by occasional relapses, remissions, and plateaus. Transition to SPMS from RRMS usually occurs after 10 to 20 years.
- Primary progressive MS (PPMS) occurs in approximately 10% of patients with MS. Patients have a continuous and gradual decline in function without evidence of acute attacks.
- Clinically isolated syndrome (CIS) refers to the first episode of neurologic symptoms that lasts at least 24 hours and is caused by inflammation or demyelination in the CNS. Patients who experience CIS may or may not develop MS (National MS Society 2025[a], Olek and Howard 2026[a]).

An estimated 1 million adults in the United States (U.S.) are affected by MS. Most patients are diagnosed between the ages of 20 and 50 years; MS is approximately 3 times more common in women than men (National MS Society 2025[b]). Pediatric-onset MS is rare, and most cases have a relapsing-remitting course (Otallah et al 2018).

The approach to treating MS includes the management of symptoms, treatment of acute relapses, and utilization of disease-modifying therapies (DMTs) to reduce the frequency and severity of relapses, reduce lesions on MRI scans, and possibly delay disease and disability progression (Rae-Grant et al 2018). The American Academy of Neurology (AAN), the European Committee for Treatment and Research of Multiple Sclerosis (ECTRIMS) and the European Academy of Neurology (EAN) guidelines recommend initiation of DMTs early in the patient's disease course (Montalban et al 2018, Rae-Grant et al 2018). These therapies may delay the progression from CIS to clinically definite MS (CDMS). The AAN and the Association of British Neurologists guidelines support access to available DMTs for patients with MS. While there are no precise algorithms to determine the order of product selection, therapy should be individualized and patients' clinical response and tolerability to medications should be monitored (Rae-Grant et al 2018, Rashid et al 2025).

Clinical Evidence

Briumvi (ublituximab-xiiy)

The efficacy and safety of ublituximab were evaluated in 2 identical Phase 3, 96-week, randomized, double-blind, double-dummy, active-controlled trials: ULTIMATE 1 and ULTIMATE 2 (Steinman et al 2022). Both trials enrolled patients 18 to 55 years of age with relapsing MS and randomized patients to receive IV ublituximab (150 mg infused over 4 hours on day 1 followed by 450 mg infused over 1 hour on day 15 and at weeks 24, 48, and 72) or oral teriflunomide (14 mg once daily).

- In ULTIMATE 1 (N = 549), the adjusted ARR over 96 weeks was 0.08 in the ublituximab group and 0.19 in the teriflunomide group (rate ratio, 0.41; 95% CI, 0.27 to 0.62; $p < 0.001$).
- In ULTIMATE 2 (N = 545), the adjusted ARR over 96 weeks was 0.09 in the ublituximab group and 0.18 in the teriflunomide group (rate ratio, 0.51; 95% CI, 0.33 to 0.78; $p = 0.002$).
- In a pooled analysis of the 2 trials, worsening of disability was not significantly different between treatment groups at any time point (week 12: 5.2% with ublituximab and 5.9% with teriflunomide; HR, 0.84; 95% CI, 0.50 to

1.41; p = 0.51; week 24: 3.3% with ublituximab and 4.8% with teriflunomide; HR, 0.66; 95% CI, 0.36 to 1.21; p not provided).
- In a pooled safety analysis, infusion-related reactions occurred in 47.7% of patients receiving ublituximab; other common AEs with ublituximab included headache, nasopharyngitis, pyrexia, and nausea. Serious infections occurred in 5% of ublituximab recipients and 2.9% of teriflunomide recipients.

Lemtrada (alemtuzumab)
The efficacy and safety of alemtuzumab were compared to Rebif (IFNβ-1a SC) in 2 Phase 3, open-label randomized controlled trials (RCTs) in patients with relapsing forms of MS – CARE-MS I and CARE-MS II (Cohen et al 2012, Coles et al 2012). In these 2-year studies, patients were randomized to alemtuzumab for 5 consecutive days followed by a 3-consecutive day treatment course 12 months later, or to Rebif (IFNβ-1a SC) 44 mcg 3 times weekly after an initial dosage titration. All patients received methylprednisolone 1 g IV for 3 consecutive days at the initiation of treatment and at month 12.

- The CARE-MS I trial enrolled treatment-naïve patients with MS (N = 581) who were high functioning based on the requirement of a score of 3 or lower on the EDSS. Patients (N = 840) enrolled in the CARE-MS II trial had experienced at least 1 relapse while on IFNβ or glatiramer acetate after at least 6 months of treatment. Patients were required to have an EDSS score of ≤ 5.
- The co-primary endpoints for both trials were the relapse rate and the time to 6-month sustained accumulation of disability.
- In the CARE-MS I trial, alemtuzumab reduced the risk of relapse by 55% compared to IFNβ-1a SC ($p < 0.0001$). Relapses were reported in 22% of alemtuzumab-treated patients and 40% of IFNβ-1a SC patients over 2 years. The proportion of patients having sustained accumulation of disability over 6 months was not significantly different between alemtuzumab (8%) vs IFNβ-1a SC (11%) ($p = 0.22$).
- In the CARE-MS II trial, alemtuzumab significantly reduced the relapse rate and sustained accumulation of disability compared to IFNβ-1a SC. The relapse rate at 2 years was reduced by 49% with alemtuzumab ($p < 0.0001$). The percent of patients with sustained accumulation of disability confirmed over 6 months was 13% with alemtuzumab and 20% with IFNβ-1a SC, representing a 42% risk reduction with alemtuzumab ($p = 0.0084$).
- Both studies evaluated MRI outcomes, specifically the median percent change in T2 hyperintense lesion volume from baseline. Neither study found a significant difference between the 2 drugs for this measure.
- During extension studies of CARE-MS I and CARE-MS II, approximately 80% of patients previously treated with alemtuzumab did not require additional treatment during the first year of the extension study (Garnock-Jones 2014).

A Cochrane review that compared the efficacy, tolerability, and safety of alemtuzumab vs IFNβ-1a in the treatment of RRMS identified 3 RCTs with 1694 total patients. In the alemtuzumab 12 mg/day group, the results showed statistically significant differences in reducing relapses (RR, 0.60; 95% CI, 0.52 to 0.70); preventing disease progression (RR, 0.60; 95% CI, 0.45 to 0.79); and developing new T2-weighted lesions on MRI (RR, 0.75; 95% CI, 0.61 to 0.93) after 24- and 36-month follow-up, but found no statistically significant difference in the changes of EDSS score (MD, -0.35; 95% CI, -0.73 to 0.03). The most frequently reported AEs with alemtuzumab were infusion-associated reactions, infections, and autoimmune events (Zhang et al 2017).

A similar Cochrane review compared the benefits and harms of alemtuzumab monotherapy and combination therapy in patients with MS. The authors did not identify additional clinical trials; they also assessed the CARE-MS I, CARE-MS II, and CAMMS223 trials. Data were insufficient to describe impact on quality of life (QOL) (Riera et al 2023).

Ocrevus (ocrelizumab)
The Phase 3 clinical development program for ocrelizumab (ORCHESTRA) included 3 studies: OPERA I, OPERA II, and ORATORIO (Hauser et al 2017, Montalban et al 2017).

OPERA I and OPERA II were 2 identically-designed, 96-week, Phase 3, active-controlled, double-blind, double-dummy, multicenter, parallel-group RCTs that evaluated the efficacy and safety of ocrelizumab 600 mg administered as an IV infusion given as two 300 mg infusions separated by 2 weeks for dose 1 and then as a single 600 mg infusion every 6

months for subsequent doses compared with Rebif (IFN β -1a) 44 mcg SC 3 times weekly in 1656 patients with relapsing MS (Hauser et al 2017, ClinicalTrials.gov Website).

- Ocrelizumab achieved statistically significant reductions in the primary endpoint, ARR, vs Rebif (IFN β -1a SC).
    - OPERA I (0.16 vs 0.29; 46% lower rate with ocrelizumab; p < 0.001)
    - OPERA II (0.16 vs 0.29; 47% lower rate with ocrelizumab; p < 0.001)
- In pre-specified pooled analyses (secondary endpoints), the percentage of patients with disability progression confirmed at 12 weeks was statistically significantly lower with ocrelizumab vs Rebif (9.1% vs 13.6%; HR, 0.60; 95% CI, 0.45 to 0.81; p < 0.001). The results were similar for disability progression confirmed at 24 weeks (6.9% vs 10.5%; HR, 0.60; 95% CI, 0.43 to 0.84; p = 0.003). The percentages of patients with disability improvement confirmed at 12 weeks were 20.7% in the ocrelizumab group vs 15.6% in the Rebif group (33% higher rate of improvement with ocrelizumab; p = 0.02). In the open-label extension over 6.5 years of follow-up, patients who received ocrelizumab throughout the trials had a significantly delayed time to reach EDSS ≥ 6.0 (requiring a walking aid) confirmed for ≥ 24 weeks compared to those who received Rebif then switched to open-label ocrelizumab (HR, 0.32; 95% CI, 0.16 to 0.64; p < 0.001) (Giovannoni et al 2022).
- The mean number of Gd-enhancing lesions per T1-weighted MRI scan, a secondary endpoint, was statistically significantly reduced with ocrelizumab vs Rebif.
    - OPERA I: 0.02 vs 0.29 (rate ratio, 0.06; 95% CI, 0.03 to 0.10; 94% fewer lesions with ocrelizumab; p < 0.001)
    - OPERA II: 0.02 vs 0.42 (rate ratio, 0.05; 95% CI, 0.03 to 0.09; 95% fewer lesions with ocrelizumab; p < 0.001)

ORATORIO was an event-driven, Phase 3, double-blind, multicenter, placebo-controlled (PC), RCT evaluating the efficacy and safety of ocrelizumab 600 mg administered by IV infusion every 6 months vs placebo in 732 people with PPMS (Montalban et al 2017, ClinicalTrials.gov Website). Double-blind treatment was administered for a minimum of 5 doses (120 weeks) until the occurrence of ~253 events of disability progression in the trial cohort that was confirmed for at least 12 weeks.

- For the primary endpoint, the percentages of patients with 12-week CDP were 32.9% with ocrelizumab vs 39.3% with placebo (HR, 0.76; 95% CI, 0.59 to 0.98; p = 0.03).
- The percentages of patients with 24-week CDP, a secondary endpoint, were 29.6% with ocrelizumab vs 35.7% with placebo (HR, 0.75; 95% CI, 0.58 to 0.98; p = 0.04).
- Additional secondary endpoints included changes in the T25FW, the total volume of hyperintense brain lesions on T2-weighted MRI, and brain volume loss.
    - The proportion of patients with 20% worsening of the T25FW confirmed at 12 weeks was 49% in ocrelizumab-treated patients compared to 59% in placebo-treated patients (25% risk reduction).
    - From baseline to Week 120, the total volume of hyperintense brain lesions on T2-weighted MRI decreased by 3.37% in ocrelizumab-treated patients and increased by 7.43% in placebo-treated patients (p < 0.001).
    - From weeks 24 to 120, the percentage of lost brain volume was 0.90% with ocrelizumab vs 1.09% with placebo (p = 0.02).

Ocrelizumab and hyaluronidase-ocsq was approved based on the data evaluating IV ocrelizumab (OPERA I, OPERA II, ORATORIO) in addition to results from the Phase 3 OCARINA II study conducted in adult patients with relapsing MS or PPMS. Studies demonstrate comparable exposure between SC ocrelizumab and hyaluronidase-ocsq and IV ocrelizumab (Ocrevus Zunovo prescribing information 2026, Newsome et al 2025).

Place in therapy

The American Academy of Neurology (AAN) performed a systematic review that included 20 Cochrane reviews and 73 additional articles in order to assess the available evidence on initiation, switching, and stopping DMTs in patients with MS (Rae-Grant et al 2018). The main recommendations were as follows:

- Starting DMT

- Discuss the benefits and risks of DMTs in those with a single demyelinating event and ≥ 2 brain lesions with imaging characteristics consistent with MS (Level B). After discussing the risks and benefits, prescribe DMTs to patients who elect to start therapy (Level B).
- Offer DMTs to people with relapsing forms of MS with recent clinical relapses or MRI activity (Level B).
- Monitor the reproductive plans of patients with MS and counsel regarding reproductive risks and use of birth control during DMT those of childbearing potential (Level B). Counsel men with MS on their reproductive plans regarding treatment implications before initiating treatment with teriflunomide (Level B).
- Do not prescribe mitoxantrone to people with MS, unless the potential therapeutic benefits greatly outweigh the risks (Level B).
- Prescribe alemtuzumab, fingolimod, or natalizumab for people with highly active MS (Level B).
- Consider initiating natalizumab treatment in people with MS with positive anti-John Cunningham virus (JCV) antibody indices > 0.9 only when there is a reasonable chance of benefit with low risk of PML (Level C).
- Offer ocrelizumab to patients with PPMS who are likely to benefit from this therapy, unless there are risks of treatment that outweigh the benefits (Level B).

- Switching DMTs
  - Discuss switching from one DMT to another in patients who have been using a DMT long enough for the treatment to take full effect and are adherent to their therapy when they experience ≥ 1 relapse, develop ≥ 2 unequivocally new MRI-detected lesions, or demonstrate increased disability on examination over a 1-year period of using a DMT (Level B).
  - Evaluate the degree of disease activity, adherence, AE profiles, and mechanism of action of DMTs when switching DMTs in patients with breakthrough disease activity during DMT use (Level B).
  - Discuss a change to non-injectable or less frequently injected DMTs in people with MS who report intolerable discomfort with the injections or those who report injection fatigue (Level B).
  - Discuss a medication switch with people with MS for whom these AEs negatively influence adherence (Level B).
  - Monitor laboratory abnormalities found on requisite laboratory surveillance (as outlined in the medication's package insert) in people with MS who are using a DMT (Level B). Discuss switching DMTs or reducing dosage or frequency (where there are data on different doses) when there are persistent abnormalities (Level B).
  - Counsel patients receiving natalizumab, fingolimod, ocrelizumab, and dimethyl fumarate about the PML risk associated with these agents (Level B). Discuss switching to a DMT with a lower PML risk with people with MS taking natalizumab who are or who become JCV antibody-positive, especially with a JCV antibody index > 0.9 while on therapy (Level B).
  - Counsel patients that new DMTs without long-term safety data have an undefined risk of malignancy and infection (Level B). If a patient develops a malignancy while using a DMT, promptly discuss switching to an alternate DMT, especially for people with MS using fingolimod, teriflunomide, alemtuzumab, or dimethyl fumarate (Level B). People with MS with serious infections potentially linked to their DMTs should switch DMTs (Level B).
  - Check for natalizumab antibodies in people with MS who have infusion reactions before subsequent infusions, or in people who experience breakthrough disease activity with natalizumab use (Level B). Switch DMTs in patients with persistent natalizumab antibodies (Level B).
  - Counsel people with MS considering natalizumab discontinuation that there is an increased risk of MS relapse or MRI-detected disease activity within 6 months of discontinuation (Level A). Physicians and people with MS choosing to switch from natalizumab to fingolimod should initiate treatment within 8 to 12 weeks after natalizumab discontinuation (for reasons other than pregnancy or pregnancy planning) to diminish the return of disease activity (Level B).
  - Discontinue DMTs during pregnancy if accidental exposure occurs, unless the risk of MS activity during pregnancy outweighs the risk associated with the specific DMT during pregnancy (Level B). Do not initiate DMTs during pregnancy unless the risk of MS activity outweighs the risk associated with the specific DMT during pregnancy (Level B).

- Stopping DMTs
    - In people with RRMS who are stable on DMT and want to discontinue therapy, counsel patients regarding the need for ongoing follow-up and periodic reevaluation (Level B). Advocate that people with MS who are stable (that is, those with no relapses, no disability progression, and stable imaging) on DMT should continue their current DMT unless an off-therapy trial is warranted (Level B).
    - Assess the likelihood of future relapse in individuals with SPMS by assessing patient age, disease duration, relapse history, and MRI-detected activity (eg, frequency, severity, time since most recent relapse or Gd-enhanced lesion) (Level B). Advise discontinuation of DMT in people with SPMS who do not have ongoing relapses (or Gd-enhanced lesions on MRI activity) and have not been ambulatory (EDSS 7 or greater) for at least 2 years (Level C).
    - Review the associated risks of continuing DMTs vs those of stopping DMTs in people with CIS using DMTs who have not been diagnosed with MS (Level B).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

BRIUMVI (ublituximab-xiiy) injection is a CD20-directed cytolytic antibody 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.

LEMTRADA (alemtuzumab) injection is a CD52-directed cytolytic monoclonal antibody indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease, in adults. Because of its safety profile, the use of Lemtrada should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

OCREVUS (ocrelizumab) injection is a CD20-directed cytolytic antibody 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.

OCREVUS ZUNOVO (ocrelizumab and hyaluronidase-ocsq) injection is a CD20-directed cytolytic antibody 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.

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Policy History/Revision Information

Date	Summary of Changes
12/13/2023	Approved by OptumRx P&T Committee
4/17/2024	Annual Review. Updated references.
4/16/2025	Annual Review. Updated references.
5/15/2025	Added Ocrevus Zunovo to policy. Updated criteria, billing codes, background section, and references to reflect this addition.
5/14/2026	Annual Review. Updated background billing codes, background section, and references.

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. The insurance reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

OptumRx may also use tools developed by third parties to assist us in administering health benefits. OptumRx Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

Nondiscrimination & Language Access Policy

Discrimination is Against the Law. Aspirus Health Plan, Inc. complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex, (including sex characteristics, including intersex traits; pregnancy or related conditions; sexual orientation, gender identity and sex stereotypes), consistent with the scope of sex discrimination described at 45 CFR § 92.101(a)(2). Aspirus Health Plan, Inc. does not exclude people or treat them less favorably because of race, color, national origin, age, disability, or sex.

Aspirus Health Plan, Inc.:
Provides people with disabilities reasonable modifications and free appropriate auxiliary aids and services to communicate effectively with us, such as:

- Qualified sign language interpreters.
- Written information in other formats (large print, audio, accessible electronic formats, other formats).

Provides free language assistance services to people whose primary language is not English, which may include:

- Qualified interpreters.
- Information written in other languages.

If *you* need reasonable modifications, appropriate auxiliary aids and services, or language assistance services, contact the Nondiscrimination Grievance Coordinator at the address, phone number, fax number, or email address below.

If *you* believe that Aspirus Health Plan, Inc. has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, *you* can file a *grievance* with:

Nondiscrimination Grievance Coordinator
Aspirus Health Plan, Inc.
PO Box 1890
Southampton, PA 18966-9998
Phone: 1-866-631-5404 (TTY: 711)
Fax: 763-847-4010
Email: customerservice@aspirushealthplan.com

You can file a *grievance* in person or by mail, fax, or email. If *you* need help filing a *grievance*, the Nondiscrimination Grievance Coordinator is available to help *you*.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1.800.368.1019, 800.537.7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html. This notice is available at Aspirus Health Plan, Inc.'s website: https://aspirushealthplan.com/webdocs/70021-AHP-NonDiscrim_Lang-Assist-Notice.pdf.

Language Assistance Services

Albanian: KUJDES: Nëse flitni shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë.Telefononi në 1-800-332-6501 (TTY: 711).

Arabic تنبيه: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية متاحة لك مجاناً. اتصل بن اعلى رقم الهاتف1-800-332-6501(رقم هاتف الصم والبك : 711)

French: ATTENTION: Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1-800-332-6501 (ATS: 711).

German: ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zurVerfügung. Rufnummer: 1-800-332-6501 (TTY: 711).

Hindi: _यान द_: य_द आप ि हंदी बोलते ह_ तो आपके ि लए मु_त म_ भाषा सहायता सेवाएं उपल_ध ह_।1-800-332-6501 (TTY: 711) पर कॉल कर_।

Hmong: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1-800-332-6501 (TTY: 711).

Korean: 주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다.1-800-332-6501 (TTY: 711)번으로 전화해 주십시오.

Polish: UWAGA: Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer1-800-332-6501 (TTY: 711).

Russian: ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода.Звоните 1-800-332-6501 (телетайп: 711).

Spanish: ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al1-800-332-6501 (TTY: 711).

Tagalog: PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nangwalang bayad. Tumawag sa 1-800-332-6501 (TTY: 711).

Traditional Chinese: 注意：如果您使用繁體中文， 您可以免費獲得語言援助服務。請 致電 1-800-332-6501 (TTY: 711)

Vietnamese: CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-800-332-6501 (TTY: 711).

Pennsylvania Dutch: Wann du Deitsch (Pennsylvania German / Dutch) schwetzscht, kannscht du mitaus Koschte ebbergricke, ass dihr helft mit die englisch Schprooch. Ruf selli Nummer uff: Call 1-800-332-6501 (TTY: 711).

Lao: ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ,ໂດຍບໍ່ເສັງຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1-800-332-6501 (TTY: 711).