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Policy Number: 026.004

Title: Coverage Determination Policy for Ocrelizumab (Ocrevus)

Regions: ☒ **Texas** ☐ **Florida** ☐ **Indiana** ☐ **New Jersey** ☒ **New Mexico**

Impacted Areas:

- ☒ Network Management/Provider Services
- ☐ Member services
- ☐ Quality Management
- ☐ Credentialing
- ☐ IT
- ☐ Administration
- ☐ Compliance/delegation
- ☒ Utilization Management
- ☐ Case management
- ☐ Disease management
- ☐ Claims
- ☐ Human resources
- ☐ Finance
- ☒ Pharmacy
- ☐ ALL

Available LCD/NCD/LCA: None

Disclaimer:

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WELLMED
Doctors helping patients for more than 25 years

Title: Coverage Determination Policy for Ocrelizumab (Ocrevus)

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Coverage Policy Number: 026.004

Line of Business: Medicare Part B

Policy Type: Prior Authorization

Coverage Determination:

*Warning: All patients **should** be screened and deemed free of active Hepatitis B Virus (HBV) prior to starting therapy with Ocrevus.*

Initial/New Requests

WellMed Medical Management will cover **Ocrevus (ocrelizumab)** as medically necessary when **ALL** of the following are met:

1) The patient has a diagnosis of Primary progressive Multiple Sclerosis (PPMS) **OR** Relapsing forms of Multiple Sclerosis (MS) (e.g. clinically isolated syndrome, relapsing-remitting MS, secondary-progressive MS with relapses, progressive-relapsing MS with relapses)

2) The patient will **NOT** be given ocrelizumab in combination with any of the following,
    a) Disease modifying therapy* (e.g. interferon beta preparations, dimethyl fumarate, glatiramer acetate, natalizumab, fingolimod, cladribine, siponimod or teriflunomide, etc.).
    b) B cell targeted therapy* (e.g. rituximab, belimumab, ofatumumab)
    c) Lymphocyte trafficking blockers* (e.g. alemtuzumab, mitoxantrone)

    *See additional therapies on page 7 chart.

3) The prescribed dosage regimen is consistent with the FDA-approved dosing

Renewal/Continuation of Therapy Requests

WellMed Medical Management will cover **Ocrevus (ocrelizumab)** as medically necessary when **ALL** of the following are met:

1) Documentation of positive clinical response to Ocrelizumab therapy

2) The patient will NOT be given ocrelizumab in combination with any of the following,

   a) Disease modifying therapy* (e.g. interferon beta preparations, dimethyl fumarate, glatiramer acetate, natalizumab, fingolimod, cladribine, siponimod, teriflunomide, etc.).

   b) B cell targeted therapy* (e.g. rituximab, belimumab, ofatumumab)

   c) Lymphocyte trafficking blockers* (e.g. alemtuzumab, mitoxantrone)

   *See additional therapies on page 7 chart.

3) Dose is in accordance to FDA labeled dosing for indication

Note: Ocrevus is currently **unproven and not medically necessary** for the treatment of:

1. Lupus nephritis
2. Rheumatoid arthritis
3. Systemic lupus erythematosus

Dosage and Administration:

1) Multiple sclerosis, Relapsing Forms & Primary progressive multiple sclerosis (PPMS)

- Initial doses: 300 mg intravenous on day 1, followed by 300 mg intravenous 2 weeks later
- Renewal doses: 600 mg intravenous once every 6 months

General Background:

Ocrevus® (Ocrelizumab) is an immune-suppressing humanized monoclonal antibody designed to target CD20 B-cell surface antigens. Ocrelizumab selectively binds to cell surface to deplete CD20-expressing B-cells through antibody-dependent cellular phagocytosis, antibody-dependent cellular cytotoxicity and complement-mediated cytolysis.

Ocrelizumab is indicated for the treatment of Relapsing Multiple Sclerosis (RMS) and Primary progressive multiple sclerosis (PPMS) in adult patients. Safety and effectiveness of ocrelizumab in pediatric patients have not been established.

Ocrelizumab is contraindicated in patients with active hepatitis B virus infection and / or patients with history of life–threatening infusion reaction to ocrelizumab. Concomitant use of live-attenuated and live vaccines are not recommended during ocrelizumab therapy. It is recommended to complete require immunizations at least six weeks prior to initiation of ocrelizumab. All patients should be screened for hepatitis B virus prior to initiation of treatment.

National Multiple Sclerosis (MS) Society: Types of MS[13]

1. **Primary Progressive MS (PPMS)**

   PPMS is characterized by worsening neurologic function (accumulation of disability) from the onset of symptoms, without early relapses or remissions. PPMS can be further characterized as either active (with an occasional relapse and/or evidence of new MRI activity over a specified period of time) or not active, as well as with progression (evidence of disability accrual over time, with or without relapse or new MRI activity) or without progression.

   PPMS involves much less inflammation of the type seen in relapsing MS. As a result, people with PPMS tend to have fewer brain lesions (also called plaques) than people with relapsing MS and the lesions tend to contain fewer inflammatory cells. People with PPMS also tend to have more lesions in the spinal cord than in the brain.

2. **Progressive-relapsing multiple sclerosis (PRMS)**

   PRMS is defined steadily worsening neurologic function from the beginning with occasional relapses in the 1996 disease-course definitions. The International Advisory Committee on Clinical Trials of MS in 2013 revised courses has stated that Individuals who were previously diagnosed with progressive-relapsing MS would now be considered primary progressive: active (at the time of relapses or new MRI lesions) or not active.

3. **Relapsing-Remitting MS (RRMS)**

   RRMS – the most common disease course – is characterized by clearly defined attacks of new or increasing neurologic symptoms. These attacks – also called relapses or exacerbations – are followed by periods of partial or complete recovery (remissions). During remissions, all

symptoms may disappear, or some symptoms may continue and become permanent. However, there is no apparent progression of the disease during the periods of remission.

RRMS can be further characterized as either active (with relapses and/or evidence of new MRI activity over a specified period of time) or not active, as well as worsening (a confirmed increase in disability following a relapse) or not worsening. Approximately 85 percent of people with MS are initially diagnosed with RRMS.

While RRMS is defined by attacks or relapses of new MS symptoms, progressive forms of MS involve fewer attacks. Most people with RRMS are usually diagnosed in their 20s and 30s (although it can occur in childhood or later adulthood), while PPMS is typically diagnosed during the 40s or 50s.The transition from RRMS to SPMS generally occurs in people who have been living with RRMS for at least 10 years.

4. **Clinically isolated syndrome (CIS)**

CIS is one of the MS disease courses. CIS refers to a first episode of neurologic symptoms that lasts at least 24 hours and is caused by inflammation or demyelination (loss of the myelin that covers the nerve cells) in the central nervous system (CNS). CIS can be either monofocal or multifocal:

- **Monofocal episode**: The person experiences a single neurologic sign or symptom — for example, an attack of optic neuritis — that is caused by a single lesion.
- **Multifocal episode**: The person experiences more than one sign or symptom — for example, an attack of optic neuritis accompanied by numbness or tingling in the legs — caused by lesions in more than one place.

Based upon clinical symptoms alone, CIS and MS may appear the same. In both, damage to the myelin sheath (demyelination) interferes with the way nerve impulses are carried from the brain, resulting in neurologic symptoms.

The episode usually has no associated fever or infection and is followed by a complete or partial recovery. Individuals who experience CIS may or may not go on to develop MS.

A person with CIS, by definition, is experiencing the first episode of symptoms caused by inflammation and demyelination in the CNS; a person with MS has experienced more than one episode.

With CIS, an MRI may demonstrate damage only in the area responsible for the current symptoms; with MS, there may be multiple lesions on MRI in different areas of the brain.

According to the 2017 revisions to the diagnostic criteria, when CIS is accompanied by evidence on MRI that another episode has occurred, the diagnosis of MS can be made. The presence of oligoclonal bands in a person's cerebrospinal fluid can also help make the diagnosis.

5. Secondary Progressive MS (SPMS)

SPMS follows an initial relapsing-remitting course. Some people who are diagnosed with RRMS will eventually transition to a secondary progressive course in which there is a progressive worsening of neurologic function (accumulation of disability) over time. SPMS can be further characterized as either active (with relapses and/or evidence of new MRI activity during a specified period of time) or not active, as well as with progression (evidence of disability accrual over time, with or without relapses or new MRI activity) or without progression.

Prior to the availability of the approved disease-modifying therapies, studies indicated that 50 percent of those diagnosed with relapsing-remitting MS (RRMS) would transition to secondary-progressive MS (SPMS) within 10 years, and 90 percent would transition within 25 years.

While MS experts agree that the medications have an impact on disease progression, it is too soon to tell the extent to which the disease-modifying treatments alter or delay the transition to SPMS

Additional therapies for MS*
Avonex (interferon beta 1a)
Betaseron, Extavia (interferon beta 1b)
Plegridy (peginterferon beta 1a)
Rebif (beta interferon 1a)
Lemtrada (alemtuzumab)
Mavenclad (cladribine)
Tecifidera (dimethyl fumarate)
Vumerity (diroximel fumarate)
Bafiertam (monomethyl fumarate)
Gilenya (fingolimod)
Glatopa, Copaxone (glatiramer acetate)
Mayzent (siponimod)
Tysabri (natalizumab)
Kesimpta (ofatumumab)
Zeposia (ozanimod)
Ponvory (ponesimod)
Aubagio (teriflunomide)
Novantrone (mitoxantrone)

*Note: This is NOT an all-inclusive list

Clinical Evidence:

The efficacy of Ocrevus™ in patients with Relapsing forms of Multiple sclerosis (RMS) was demonstrated in two identical clinical trials. The studies were randomized, double-blind, double-dummy, active comparator-control clinical trial. The studies lasted for 96 weeks. Patients in both trials (study 1 and study 2) were treated with Ocrevus™ 300 mg 2 weeks apart, then 600 mg every 24 weeks followed by placebo subcutaneous injections 3 times per week. Patients on the active comparator were treated with Rebif 44 mcg subcutaneous injections 3 times per week and placebo IV infusions every 24 weeks.

The primary outcome measures annualized relapse rate (ARR) while the secondary outcome included proportion of patients with confirmed disability progression. Progression of disability was defined as an increase of 1 point or more from the baseline Expanded Disability Status Scale (EDSS) score resulting from multiple sclerosis when the baseline EDSS score was 5.5 or less, or 0.5 points or more when the baseline EDSS score was above 5.5. Disability progression was confirmed at week 12 visit after the initial documentation of neurological worsening.

Study 1 randomized 410 patients to Ocrevus and 411 to Rebif. Annualized relapse rate was 0.156 in Ocrevus and 0.292 in Rebif. Relative reduction was 46% ($p < 0.0001$). Proportion of relapse-free patients was 83% in Ocrevus and 71% in Rebif. Study 2 randomized 417 patients to Ocrevus and 418 to Rebif. Annualized relapse rate was 0.155 in Ocrevus and 0.290 in Rebif. Relative reduction was 47% ($p < 0.0001$). Proportion of relapse-free patients was 82% in Ocrevus and 72% in Rebif.

In both studies, the proportion of patients with 12-week confirmed disability progression was 9.8% in Ocrevus vs 15.2% in Rebif. Risk reduction (Pooled) was 40% ($P = 0.0006$). The study concluded that Ocrevus significantly lowered the annualized relapse rate and the proportion of patients with disability progression confirmed at 12 weeks after onset compared to Rebif.

Efficacy of Ocrevus in patients with Primary progressive multiple sclerosis (PPMS) was studied in a randomized, double-blind, placebo-controlled clinical trial. Patients received Ocrevus 600 mg or placebo 2 300 mg intravenous infusions 2 weeks apart every 24 weeks for at least 120 weeks. The primary outcome was the time to onset of disability progression resulting from multiple sclerosis confirmed to be present at the next neurological assessment at least 12 weeks later. Progression of disability was defined as an increase of 1 point or more from the EDSS score resulting from multiple sclerosis when the baseline EDSS score was 5.5 or less, or 0.5 points or more when the baseline EDSS score was above 5.5. Patients who discontinued participation in the study before their next assessment after an onset of disability progression are also confirmed as having disability progression.

The study randomized 488 patients to Ocrevus and 244 to placebo. The average age of patients was 45. Proportion of patients with 12-weeks confirmed disability progression was 32.9 % in Ocrevus treated patients' vs 39.3% in placebo. Risk reduction was 24%; $P = 0.0321$. The study concluded that Ocrevus treated patients had significantly longer time to onset of disability progression confirmed at 12 weeks after onset than placebo treated patients.

Coding Information

HCPCS Code:	Description:
J2350	Ocrevus (ocrelizumab)

Acronyms:

MSR = Multiple sclerosis, Relapsing Forms; PPMS = Primary progressive multiple sclerosis;

EDSS = Expanded Disability Status Scale; FDA = Food and Drug Administration;

ARR = Annualized relapse rate; IV = Intravenous

CIS = Clinically isolated syndrome RRMS = Relapsing- remitting multiple sclerosis

SPMS = Secondary progressive multiple sclerosis

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