Highmark Commercial Medical Policy-PA/WV/DE/NY

Medical Policy:	I-171-01~~6~~7
Topic (or Title):	Ocrelizumab (Ocrevus) and Ocrelizumab and hyaluronidase-ocsq (Ocrevus Zunovo)
Section:	Injections
Effective Date:	~~December 15, 2025~~ September 1, 2026
Issued Date:	~~December 15, 2025~~ September 1, 2026
Last Revision Date:	~~October 2025~~ May 2026
Annual Review:	October 2025

Ocrelizumab (Ocrevus®) and ocrelizumab and hyaluronidase-ocsq (Ocrevus Zunovo™) are CD20-directed cytolytic antibodies indicated for relapsing or primary progressive forms of multiple sclerosis (MS).

Ocrelizumab and hyaluronidase-ocsq (Ocrevus Zunovo) is a combination of ocrelizumab and hyaluronidase in a subcutaneous formulation that is given by a healthcare professional. These two products are different formulations and cannot be used interchangeably.

Policy Position

Ocrelizumab and ocrelizumab and hyaluronidase-ocsq (Ocrevus Zunovo) may be considered medically necessary for the treatment of **EITHER** of the following conditions:

- Relapsing forms of MS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, when **ALL** of the following are met:
  - Adults 18 years of age or older; **and**
  - A diagnosis of relapsing forms of multiple sclerosis as defined by an MRI of the brain showing abnormalities consistent with MS; **and**
  - Prescribed by, or in consultation with, a neurologist or provider who specializes in the treatment of MS; **and**
  - Does not have an active Hepatitis B virus infection; **and**
  - Individual will not receive a live vaccine for at least four (4) weeks prior to and during treatment with Ocrevus or Ocrevus Zunovo; **and**
  - Individual is not receiving Ocrevus or Ocrevus Zunovo in combination with another disease modifying therapy for MS; **or**
- Primary progressive MS when **ALL** of the following are met:
  - Adults 18 years of age; **and**
  - Individual will not receive a live vaccine for at least four (4) weeks prior to and during treatment with Ocrevus or Ocrevus Zunovo; **and**
  - A diagnosis of primary progressive multiple sclerosis (PPMS) based on the McDonald criteria:
    - Note: McDonald criteria defined as:
      - One or more years in which neurologic symptoms typical of multiple sclerosis progressively worsen and at least **TWO** (2) of the following:
        - Evidence of lesion dissemination in space in the brain based on greater than or equal to one (1) T2 lesions in at least one (1) area characteristic for MS periventricular, juxtacortical, or infratentorial; Gadolinium enhancement of lesions is not required; **or**

        - Evidence of lesion dissemination in space in the spinal cord based on greater than or equal to two (2) T2 lesions in the cord (Gadolinium enhancement of lesions is not required); **or**
        - A documented history or presence of an elevated CSF IgG index or CSF oligoclonal band; **and**
    - Does not have an active Hepatitis B virus infection; **and**
    - Individual is not receiving Ocrevus or Ocrevus Zunovo in combination with another disease modifying therapy for MS; **and**
- Initial authorization will be for a period of up to 12 months.

Reauthorization Criteria

Continuation of therapy with ocrelizumab (Ocrevus) and ocrelizumab and hyaluronidase-ocsq (Ocrevus Zunovo) may be considered medically necessary when all the following criteria are met;

- Individual has documented positive clinical response (e.g. reduction in annualized relapse rates, confirmed delay or improvement of disability progression, reduction in number or volume of lesions on MRI,); **and**
- Individual is not receiving -Ocrevus or Ocrevus Zunovo in combination with another disease modifying therapy for MS; **and**
- Reauthorization will be for a period of up to 12 months

The use of ocrelizumab (Ocrevus) and ocrelizumab and hyaluronidase-ocsq (Ocrevus Zunovo) not meeting the criteria as indicated in this policy is considered not medically necessary.

Procedure Codes

J2350	J2351

Ocrelizumab (Ocrevus) or ocrelizumab and hyaluronidase-ocsq (Ocrevus Zunovo) may be considered medically necessary for individuals 18 years of age and older when applicable clinical criteria for individual medication policies are met and when administered in a Lower Level of Care. ~~in a physician's office not affiliated with a hospital, specialized infusion centers not affiliated with a hospital or in the home.~~

~~Outpatient facility (Outpatient Hospital IV Infusion Department or Hospital-based Outpatient Clinical Level of Care) administration may be considered medically necessary if **ANY** of the following criteria are present to indicate the member is medically unstable for infusions in settings other than an outpatient facility setting:~~

The Highest Level of Care Site may be considered medically necessary if the following criteria are present to indicate the member is medically unstable for infusions in settings other than a Highest Level of Care Site:

- Individual's home is considered unsuitable for care by the home infusion provider; or
- Individual is physically impaired and/or cognitively impaired AND a home caregiver is not available to comply with the required treatment regimen and schedule; and
- Individual requires higher level of care not feasible in the Lower Level of Care Sites, as indicated by ANY of the following:
    - Individual's medical status requires enhanced monitoring beyond that which would routinely be needed for infusion therapy; or

- Previous severe adverse reaction (including but not limited to anaphylaxis, seizure, thromboembolism, myocardial infarction, renal failure) during or following administration of prescribed medication despite standard pre-medication; or
- Individual is receiving other medications that require close monitoring with a higher level of care (*e.g.*, cytotoxic chemotherapy or blood products); or
- Individual is at high risk for complications due to medication administration (*e.g.*, at risk for post-transplant complications, increased risk of infusion reactions due to presence of circulating antibodies, unstable vascular access, cardiopulmonary condition at risk for severe adverse reactions, unstable renal function with inability to safely tolerate IV volume loads, etc.); or
- Individual is at high risk for complications on their current care regimen initiating therapy or re-initiating therapy after a period of at least 6 months with no therapy.

Home health services may be considered medically necessary when utilized for the administration of home infusion therapy and when provided by licensed eligible provider. Each case will be addressed on an individual basis.

The medications identified in this policy will be considered not medically necessary if administered in an unapproved Highest Level of Care Site when an approved Highest Level of Care Site or Lowest Level of Care Site is a viable option for treatment.

- ~~Member's home is considered unsuitable for care by the home infusion provider; **or**~~
- ~~Individual's medical status requires enhanced monitoring beyond that which would routinely be needed for infusion therapy; **or**~~
- ~~Previous severe adverse reaction (including but not limited to anaphylaxis, seizure, thromboembolism, myocardial infarction, renal failure) during or following administration of prescribed medication despite standard pre-medication; **or**~~
- ~~Individual is receiving other medications that require close monitoring with a higher level of care (*e.g.*, cytotoxic chemotherapy or blood products); **or**~~
- ~~Individual is at high risk for complications due to medication administration (*e.g.*, at risk for post-transplant complications, increased risk of infusion reactions due to presence of circulating antibodies, unstable vascular access, cardiopulmonary condition at risk for severe adverse reactions, unstable renal function with inability to safely tolerate IV volume loads, etc.); **or**~~
- ~~Individual is initiating therapy or re-initiating therapy after a period of at least 6 months with no therapy; **or**~~
- ~~Physically and/or cognitively impaired **AND** a home caregiver is not available to comply with the required treatment regimen and schedule.~~

~~Home health services may be considered medically necessary when utilized for the administration of home infusion therapy and when provided by licensed eligible provider. Each case will be addressed on an individual basis.~~

~~The medications identified in this policy will be considered not medically necessary if administered in an unapproved hospital outpatient setting when an approved site of care is a viable option for treatment.~~

Procedure Codes

J2350 J2351

NOTE: In addition to the above criteria, product specific dosage and/or frequency limits may apply in accordance with the U.S. Food and Drug Administration (FDA)-approved product prescribing information, national compendia, Centers for Medicare and Medicaid Services (CMS) and other peer reviewed resources or evidence-based guidelines. Highmark may deny, in full or in part, reimbursement for utilization that does not fall within the applicable dosage and/or frequency limits.

References

1. Micromedex DrugDex Compendium®. 2025. Ocrelizumab.

2. Clinical Pharmacology™ Compendium. 2025. Tampa FL: Gold Standard, Inc. Ocrelizumab.

3. Montalban X, Hauser SL, Kappos L, et al. Ocrelizumab versus Placebo in Primary Progressive Multiple Sclerosis. *N Engl J Med*. 2017;209-20.

4. Ocrevus (Ocrelizumab) injection, for intravenous use [package insert]. Genentech, Inc. South San Francisco, CA. Revised 08/2025.

5. Gelfand J, Cree B, & Hauser S. Ocrelizumab and other CD20+ b-cell-depleting therapies in multiple sclerosis. *Neurotherapeutics*. 2017;14:835-841.

6. MCGTM Care Guidelines, 22nd edition, 2018, Home Infusion Therapy, CMT: CMT-0009(SR).

7. Soelberg Sorensen P. Safety concerns and risk management of multiple sclerosis therapies. *Acta Neurologica Scandinavica*. 2017;136(3):168-186.

8. Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *The Lancet*. 2018. 17(2):162-173.

9. Daniels K, van der Nat PB, Frequin STFM, et al. Real-world results of ocrelizumab treatment for primary progressive multiple sclerosis. *Multiple Sclerosis International*.2020:1-6.

10. Dirks P, Zingler V, Leemhuis J, et al. Design of a non-interventional post-marketing study to assess the long-term safety and effectiveness of ocrelizumab in German real world multiple sclerosis cohorts - the CONFIDENCE study protocol. *BMC Neurology*. 2020;20(1):1-9.

11. Ocrelizumab In: AHFS Drug Information Online Electronic Medical Library. Bethesda, MD: American Society of Health-System Pharmacists. Updated December 17, 2022.

12. Hauser SL, Kappos L, Arnold DL, et al. Five years of ocrelizumab in relapsing multiple sclerosis: OPERA studies open-label extension. *Neurology*. 2020;95(13):e1854-e1867.

13. Hughes R, Whitley L, Fitovski K, et al. COVID-19 in ocrelizumab-treated people with multiple sclerosis. *Mult Scler Relat Disord*. 2021;49:102725. doi: 10.1016/j.msard.2020.102725.

14. Ocrevus Zunovo™ (ocrelizumab and hyaluronidase-ocsq) injection, for subcutaneous use [package insert]. Genentech, Inc. South San Francisco, CA. Revised 08/2025.

15. Newsome S, Krzystanek E, Selmaj K, et al. OCARINA II, Phase III Study: Results of Subcutaneous Ocrelizumab Administration in Patients with Multiple Sclerosis. *Neurology*. 2024;102(17).

Related Policies

Please refer to Medical Policy I-151, Site of Care, for additional information.

Covered Diagnosis Codes for Procedure Codes J2350, J2351

G35.A	G35.B0	G35.B1	G35.B2	G35.C0	G35.C1	G35.C2
G35.D						

Place of Service: Outpatient-Infusion

Evidence-based guidelines support the administration of injectable medications in alternative sites of care such as the non-hospital physician's office, non-hospital infusion center or in the home. Administration of the injectable medications subject to this policy at alternate sites of care is based upon the professional judgment of the provider, and takes into account the clinical appropriateness for each individual member. Requests for administration of any dose of the drugs listed in this policy received from a hospital-based facility, physician's office or specialized infusion center will be assessed for meeting the policy exception criteria based on the clinical documentation provided by the requesting practitioner.

The policy position applies to all commercial lines of business

If you need these services, contact the Civil Rights Coordinator.

If you believe that the Claims Administrator/Insurer 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: Civil Rights Coordinator, P.O. Box 22492, Pittsburgh, PA 15222, Phone: 1-866-286-8295, TTY: 711, Fax: 412-544-2475, email: CivilRightsCoordinator@highmarkhealth.org. You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights 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.

Insurance or benefit/claims administration may be provided by Highmark, Highmark Choice Company, Highmark Coverage Advantage, Highmark Health Insurance Company, First Priority Life Insurance Company, First Priority Health, Highmark Benefits Group, Highmark Select Resources, Highmark Senior Solutions Company or Highmark Senior Health Company, all of which are independent licensees of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield plans.

ATTENTION: If you speak English, language assistance services, free of charge, are available to you. Call the number on the back of your ID card (TTY: 711).

ATENCIÓN: Si usted habla español, servicios de asistencia lingüística, de forma gratuita, están disponibles para usted. Llame al número en la parte posterior de su tarjeta de identificación (TTY: 711).

请注意：如果您说中文，可向您提供免费语言协助服务。

请拨打您的身份证背面的号码（TTY：711）。

CHÚ Ý: Nếu quý vị nói tiếng Việt, chúng tôi cung cấp dịch vụ hỗ trợ ngôn ngữ miễn phí cho quý vị. Xin gọi số điện thoại ở mặt sau thẻ ID của quý vị (TTY: 711).

알림: 한국어를 사용하시는 분들을 위해 무료 통역이 제공됩니다. ID 카드 뒷면에 있는 번호로 전화하십시오 (TTY: 711).

ATENSYON: Kung nagsasalita ka ng Tagalog, may makukuha kang mga libreng serbisyong tulong sa wika. Tawagan ang numero sa likod ng iyong ID card (TTY: 711).

ВНИМАНИЕ: Если вы говорите по-русски, вы можете воспользоваться бесплатными услугами языковой поддержки. Позвоните по номеру, указанному на обороте вашей идентификационной карты (номер для текст-телефонных устройств (TTY): 711).

تنبيه: إذا كنت تتحدث اللغة العربية، فهناك خدمات المعاونة في اللغة المجانية متاحة لك. اتصل بالرقم الموجود خلف بطاقة هويتك (جهاز الاتصال لذوي صعوبات السمع والنطق: 711).

ATTENTION: Si c'est créole que vous connaissez, il y a un certain service de langues qui est gratis et disponible pour vous-même. Composez le numéro qui est au dos de votre carte d'identité. (TTY: 711).

ATTENTION: Si vous parlez français, les services d'assistance linguistique, gratuitement, sont à votre disposition. Appelez le numéro au dos de votre carte d'identité (TTY: 711).

UWAGA: Dla osób mówiących po polsku dostępna jest bezpłatna pomoc językowa. Zadzwoń pod numer podany na odwrocie karty ubezpieczenia zdrowotnego (TTY: 711).

ATENÇÃO: Se a sua língua é o português, temos atendimento gratuito para você no seu idioma. Ligue para o número no verso da sua identidade (TTY: 711).

ATTENZIONE: se parla italiano, per lei sono disponibili servizi di assistenza linguistica a titolo gratuito. Contatti il numero riportato sul retro della sua carta d'identità (TTY: 711).

ACHTUNG: Wenn Sie Deutsch sprechen, steht Ihnen unsere fremdsprachliche Unterstützung kostenlos zur Verfügung. Rufen Sie dazu die auf der Rückseite Ihres Versicherungsausweises (TTY: 711) aufgeführte Nummer an.

注：日本語が母国語の方は言語アシスタンス・サービスを無料でご利用いただけます。ID カードの裏に明記されている番号に電話をおかけください (TTY: 711)。

توجه : اگر شما به زبان **فارسی** صحبت می کنید، خدمات کمک زبان، به صورت رایگان، در دسترس شماست. با شماره واقع در پشت کارت شناسایی خود (TTY: 711) تماس بگیرید.