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CERTIFIED PUBLIC ACCOUNTANTS

Background

The Oregon Department of Consumer and Business Services (DCBS) Prescription Drug Affordability Board (PDAB) staff requested that Myers and Stauffer assess the clinical appropriateness of Rituxan (rituximab) being referenced as a clinical alternative to Ocrevus (ocrelizumab) within documents utilized by the PDAB for conducting an affordability review. Genentech, the manufacturer of both Rituxan and Ocrevus, has requested the Board to exclude Rituxan as an inappropriate therapeutic alternative based on their interpretation of the definition of "therapeutic alternative" in OAR 925-200-0020(2)(c):

> *Therapeutic alternative is to mean, "A drug product that contains a different therapeutic agent than the drug in question, but is FDA-approved, compendia-recognized as off-label use for the same indication, or has been recommended as consistent with standard medical practice by medical professional association guidelines to have similar therapeutic effects, safety profile, and expected outcome when administered to patients in a therapeutically equivalent dose."*

Genentech cited biological inconsistency, clinical inconsistency, and regulatory inconsistency in their request for removal.

Clinical Indications

Ocrelizumab, a CD20-directed cytolytic antibody, is FDA-approved for the treatment of relapsing forms of multiple sclerosis (MS) and primary progressive MS in adults, and relapsing-remitting MS in pediatric patients.[i]

Rituximab is a CD20-directed cytolytic antibody indicated for the treatment of Non-Hodgkin's Lymphoma (NHL) and other oncology and autoimmune disorders.[ii] It is not FDA-approved to treat MS.

Supporting Evidence for Rituxan in MS

Micromedex recognizes the off-label use of rituximab in Relapsing Remitting MS (RRMS).[iii] The strength of recommendation is Adult Class IIb: Recommended, in some cases. The strength of evidence is Category B, indicating the evidence is based on data derived from meta-analyses of randomized controlled trials with conflicting conclusions with regard to the directions and degrees of results between individual studies, randomized controlled trials that involved small numbers of patients or had significant methodological flaws, or nonrandomized studies.

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The American Academy of Neurology Practice Guideline includes rituximab in their recommendations.[iv] Their review determined that rituximab is probably more effective than placebo in decreasing the risk of relapse at one year in those with RRMS. Regarding starting treatment, the guideline recommends that clinicians should offer ocrelizumab to people with Primary Progressive MS (PPMS). The rationale for this recommendation states, "Ocrelizumab is the only DMT [disease modifying treatment] shown to alter disease progression in individuals with PPMS who are ambulatory. The RCT [randomized controlled trial] of rituximab in PPMS was promising but inconclusive." Additionally, the guidelines also state that although RCT data are unavailable, retrospective cohort data shows that when switching from natalizumab, rituximab "may result in lower rates of clinical and radiologic disease activity compared with switching to fingolimod."

The Consortium of Multiple Sclerosis Centers Best Practices in Multiple Sclerosis Therapies discusses the off-label use of rituximab:

> *Similar to the two approved anti-CD20 agents in MS (ocrelizumab and ofatumumab) rituximab binds to the CD20 antigen on B cells to induce near-complete B-cell depletion. Some studies have shown differences between rituximab and the other anti-CD20 agents in immunogenicity; effect on T cells; binding affinity; and complement activation; but it is not clear how important these differences are clinically.[…] it is clear that this agent [rituximab] has a place in MS therapy and will continue to be used clinically in many settings as a more cost-effective option among anti-CD20 agents."* [v]

The Institute for Clinical and Economic Review (ICER) published a final evidence report on treatments for MS in 2023, which included several recommendations regarding the inclusion of rituximab as a treatment option in relapsing MS (RMS), including:

> *All stakeholders have a responsibility and an important role to play in ensuring that all effective treatment options for patients with RMS, including off-label use of rituximab, are utilized in ways to help improve affordability and access and reduce health inequities. […] All stakeholders should work together to remove barriers to rituximab for the treatment of RMS, as broader use of rituximab, particularly biosimilar rituximab, could lead to better health outcomes, less financial toxicity to patients, and lessen health inequities.*[vi]

In early 2026, the MS International Federation developed evidence-based recommendations for the use of rituximab in low-resource settings. The panel recommends the use of rituximab in

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patients with RMS and active PPMS compared to no treatment or several on-label DMTs. These recommendations were based on very low certainty of evidence but provide a case for rituximab as a treatment in low-resource settings.[vii] [viii]

The National Multiple Sclerosis Society includes rituximab in its listing of medications commonly used off-label, stating that studies have demonstrated efficacy in reducing relapses, limiting new CNS inflammation, and limiting progression of MS.[ix]

A study recently published in the *New England Journal of Medicine* directly compared rituximab versus ocrelizumab in newly diagnosed RMS. Patients were randomized to receive rituximab or ocrelizumab every 6 months for 24 months, with a primary endpoint of absence of new or enlarging lesions on MRI. The study found rituximab to be noninferior to ocrelizumab with a similar incidence of serious adverse events.[x]

Conclusion

The Oregon PDAB staff agrees with Genentech's assessment that rituximab is not FDA approved for use in MS, and ocrelizumab is a preferred first-line agent in PPMS. However, its off-label use in RMS has been documented in compendia, guidelines, and trials. Based on the above information, and consistent with the definition in OAR 925-200-0020(2)(c), "*compendia-recognized as off-label use for the same indication, or has been recommended as consistent with standard medical practice by medical professional association guidelines…"* we agree that it is appropriate to include Rituxan as a therapeutic alternative to Ocrevus for consideration within the PDAB's affordability reviews.

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[i] U.S. Food & Drug Administration. *Ocrevus (ocrelizumab) Prescribing Information*. Genentech, Revised 05/2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/761053s038lbl.pdf

[ii] U.S. Food & Drug Administration. *Rituxan (rituximab) Prescribing Information*. Genentech, Revised 12/2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/103705s5467lbl.pdf

[iii] Rituximab. Merative Micromedex. Merative. Ann Arbor, MI. Accessed July 14, 2026. https://www.micromedexsolutions.com/

[iv] Rae-Grant, A., Day, G. S., Marrie, R. A., Rabinstein, A., Cree, B. A. C., Gronseth, G. S., Haboubi, M., Halper, J., Hosey, J. P., Jones, D. E., Lisak, R., Pelletier, D., Potrebic, S., Sitcov, C., Sommers, R., Stachowiak, J., Getchius, T. S. D., Merillat, S. A., & Pringsheim, T. (2018). Practice guideline recommendations summary: Disease-modifying therapies for adults with multiple sclerosis: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*, *90*(17), 777–788. https://doi.org/10.1212/WNL.0000000000005347

[v] Lublin, F. D. (Ed.). (2025). *Best practices in multiple sclerosis therapies* [Expert panel document]. Consortium of Multiple Sclerosis Centers. https://www.mscare.org/best-practices-in-multiple-sclerosis-therapies/

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[vi] Oral and Monoclonal Antibody Treatments for Relapsing Forms of Multiple Sclerosis: Final Policy Recommendations. https://icer.org/wp-content/uploads/2023/02/ICER_MS_Policy_Recommendations.pdf

[vii] Rijke N, Yamout BI, Saylor D, et al. Recommendations for the use of off-label rituximab for the treatment of multiple sclerosis in low-resource settings. Mult Scler Relat Disord. 2026; 105: 106878, doi: 10.1016/j.msard.2025.106878

[viii] MSIF off-label treatments (MOLT) panel guideline for the treatment of multiple sclerosis in low-resource settings. https://www.msif.org/wp-content/uploads/2022/11/MOLT_EtD-and-recommendations_public_301122.pdf

[ix] Medications used off label for MS. https://www.nationalmssociety.org/managing-ms/treating-ms/disease-modifying-therapies/off-label-use

[x] Torkildsen, Ø., Brustad, H. K., Høgestøl, E. A., Alstadhaug, K. B., Bhan, A., Flemmen, H. Ø., … Myhr, K.-M. (2026). Rituximab versus ocrelizumab in newly diagnosed relapsing multiple sclerosis. *New England Journal of Medicine*, *395*(1), 44–53. doi:10.1056/nejmoa2600993

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