

**Category**

Best Pharmaceutical Product

**Drug / Device Name**

Ocrevus®

**Compound/ Tech Name**

ocrelizumab

**Trade Name**

Ocrevus® (ocrelizumab)

**Date of Approval**

2019-07-16

**Indications**

- 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.

**Therapeutic Categories**

Multiple sclerosis

**Background information and need for drug/device**

Nearly 1 million people in the U.S. are living with MS. They are most often diagnosed as young or middle-aged adults — in their 20s through 40s — and experience cognitive impairment, physical disabilities and mobility issues that can significantly impact their lives.

The disease's impact on quality of life cannot be overstated; instead of focusing on building their families or careers, they contend with symptoms such as fatigue, difficulty walking, impaired vision and bladder issues. Many lose their jobs as the disease progresses due to physical and neurological impairments. It's not uncommon for people with MS to need wheelchairs, mobility aids and caregivers just to meet their daily needs.

While we've seen progress in the fight against MS, there remains no cure for the disease. Historically, MS treatments focused on reducing relapses in relapsing MS (RMS). Still, people with this form of the disease frequently had to choose between higher efficacy medicines that came with serious risks or medicines that provided limited efficacy to slow underlying, chronic disease progression.

Meanwhile, the 15% of people with MS who had the primary progressive form of the disease (PPMS) were left without a disease-modifying medicine at all. But this form is one of the most disabling forms of MS marked by steadily worsening symptoms, typically without distinct relapses or periods of remission, and are most in need of safe and effective treatment options to slow disease progression.

Before the introduction of Ocrevus, there clearly remained a significant need for an innovative medicine that offered the potential for more effective control of disease symptoms and progression so people living with MS could live more independent and fuller lives.

### **History of the development of the drug/device**

T cells were long believed to be the main culprit in the underlying biology of MS. However, based on a growing body of evidence suggesting a pivotal role for B cells in the immunopathology of MS, Dr. Stephen Hauser, then Chair of the Department of Neurology at University of California, San Francisco (UCSF) and current Director of the UCSF Weill Institute for Neurosciences, began discussions to test B-cell depletion in MS in 2001.

Dr. Hauser wanted to test this theory with an existing CD20-targeted B-cell depleting therapy; however, the MS research community was skeptical and an attempt to obtain public funding to conduct a clinical trial failed.

Genentech recognized the need for innovative medicines in MS and supported Dr. Hauser's Phase 2 studies in RMS and PPMS. Insights from these proof-of-concept studies clearly demonstrated that Dr. Hauser was onto something — selective depletion of CD20-expressing B-cells appeared to be a potential approach to treating MS.

Inspired by this compelling data, Roche and Genentech launched a large clinical trial program comprised of three Phase 3 trials – two in RMS and one in PPMS – to thoroughly test the new treatment approach with a next-generation B-cell targeting drug — the anti-CD20 antibody, Ocrevus.

The pivotal results in RMS were astounding. Inflammatory lesion activity in the brain was nearly completely suppressed, the annualized relapse rate was dramatically reduced, and disability progression was cut by nearly half when compared to interferon beta-1a. The first-ever positive data slowing disability progression in PPMS were also game-changing. When these data were initially presented at an international congress, neurologists were astonished by the compelling results.

The first-of-their-kind results led to Ocrevus being the first approved anti-CD20 medicine for MS and the first and only medicine approved in the U.S., and other countries around the world, to treat both RMS and PPMS.

### **Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition**

Our approach to targeting B cells began a new era for the MS community and has redefined our understanding of MS biology. Our trials showed that B cells play a central role in the disease, and that underlying disease progression occurs in all forms of MS.

The FDA recognized the potential of Ocrevus and granted Breakthrough Therapy designation for PPMS in Feb 2016 and a Priority Review of the licensing application for RMS and PPMS in June 2016. Ocrevus was the first and only medicine for both RMS and PPMS approved by the FDA. Five years later, it remains the only disease-modifying medicine for PPMS in the U.S.

Ocrevus' potential was proven in three Phase 3 trials.<sup>5,6</sup> In two RMS trials, Ocrevus demonstrated superior efficacy in three major markers of disease activity and progression vs. high-dose interferon beta-1a.<sup>5</sup> In the PPMS trial, Ocrevus was the first to significantly slow disability progression and reduce signs of disease activity in the brain vs. placebo.<sup>6</sup>

In all pivotal studies, the Ocrevus group experienced a low rate of serious adverse events.<sup>5,6</sup>

The RMS indication was updated in 2019 to include clinically isolated syndrome and active secondary progressive MS. A shorter, two-hour infusion was approved in 2020. We are advancing its development across more than 30 ongoing clinical trials. Long-term data continue to demonstrate a consistent benefit-risk profile for Ocrevus over nine years.

Today, Ocrevus has treated 300,000 people globally and is approved in over 100 countries. And we remain dedicated to expanding access to new patient groups with our ongoing Ocrevus trial program. We are studying higher dose and subcutaneous formulas in Phase 3 trials and the safety of Ocrevus in pregnant and breastfeeding women.

Ocrevus — and its unique mechanism of action — has transformed the MS treatment landscape.

**Please provide appropriate references (ie Pubmed links)**

Submission References:

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6 Montalban X, et al. Ocrelizumab versus Placebo in Primary Progressive Multiple Sclerosis. *New England Journal of Medicine* 2017; 376:209-220.

7 OCREVUS (ocrelizumab) Prescribing Information. Genentech, Inc., 2017.

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Attached Files:

- US Prix Galien Award submission\_22 May 2023.docx