# Ocrelizumab

Targets (1) Biointeractions (1)

## IDENTIFICATION

**Name**

Ocrelizumab

**Accession Number**

DB11988

**Type**

Biotech

**Groups**

Approved, Investigational

**Biologic Classification**

Protein Based Therapies
Monoclonal antibody (mAb)

**Description**

Ocrelizumab is a CD20-directed cytolytic antibody indicated for the treatment of patients with relapsing or primary progressive forms of multiple sclerosis. It is a second-generation recombinant humanized monoclonal IgG1 antibody that selectively targets the B lymphocytes that express the CD20 antigen. As a humanized molecule, ocrelizumab is expected to be less immunogenic with repeated infusions which improves the benefit-to-risk profile for patients with relapsing or progressive forms of MS.

Multiple sclerosis (MS) is a chronic, inflammatory, autoimmune disease of the central nervous system that leads to neurological disabilities and significantly reduced quality of life [5]. Most patients with MS experience episodes of relapses with worsening function, followed by recovery

Developed by Genentech, Roche, ocrelizumab was approved by the FDA in March 2017 under the market name Ocrevustm for intravenous injection. It was later approved by Health Canada (as Ocrevus) in August 2017, making the drug the first available treatment for PPMS in both U.S. and Canada. In clinical trials of patients with relapsing forms of MS, treatment with ocrelizumab resulted in reduced relapse rates and reduced worsening of disability compared to interferon beta-1a [5]. In phase 3 clinical trials of patients with PPMS, treatment with ocrelizumab demonstrated lower rates of clinical and MRI progression than placebo [4].

### Protein chemical formula

$C_{6494}H_{9978}N_{1718}O_{2014}S_{46}$

### Protein average weight

145000.0 Da (Approximate, glycosylated)

### Sequences

Not Available

### Synonyms

Ocrelizumab (genetical recombination)

### External IDs

PR-070769 / PR070769 / R-1594 / RG-1594

### Prescription Products

Search

| NAME | DOSAGE | STRENGTH | ROUTE | LABELLER | MARKETING START | MARKETING END | |
|---|---|---|---|---|---|---|---|
| **Ocrevus** | Injection | 300 mg/10mL | Intravenous | Genentech, Inc. | 2017-03-28 | Not applicable | |
| **Ocrevus** | Solution | 30 mg | Intravenous | Hoffmann La Roche | 2017-09-21 | Not applicable | |

Showing 1 to 2 of 2 entries

‹ ›

Antibodies, Monoclonal

Blood Proteins

CD20-directed Cytolytic Antibody

Globulins

Immunoglobulins

Immunomodulatory Agents

Immunoproteins

Proteins

Serum Globulins

**UNII**

A10SJL62JY

**CAS number**

637334-45-3

## PHARMACOLOGY

**Indication**

Indicated for the treatment of adult patients with relapsing or primary progressive forms of multiple sclerosis [Label].

**Associated Conditions**

Multiple Sclerosis, Primary Progressive

Relapsing Multiple Sclerosis (RMS)

**Pharmacodynamics**

Since ocrelizumab interferes with the CD20 assay, CD19+B-cells were used to assess B-cell counts after ocrelizumab treatment. 14 days following infusion, a reduction in CD19+B-cell counts was observed. In clinical studies, B-cell counts rose to above the lower limit of normal (LLN) or above baseline counts between infusions of ocrelizumab at least one time in 0.3% to 4.1% of patients. In

### Mechanism of action

B lymphocytes are known to contribute to the pathogenesis of MS through activation of pro-inflammatory T cells and secretion of proinflammatory cytokines. B cells may differentiate into plasma cells that can produce autoantibodies directed against myelin and cause complement-mediated attack on the myelin sheath [3]. CD20 is a cell-surface antigen found on pre-B cells, naïve and mature B cells and memory B cells. However, this activated glycosylated phosphoprotein is not expressed on haematopoietic stem cells, pro-B cells (precursors), or differentiated plasma cells [3, 4].

While the exact mechanism of ocrelizumab leading to B-cell depletion is unknown, there are several different proposed mechanisms. Upon cell surface binding to CD20-expressing B lymphocytes, ocrelizumab promotes antibody-dependent cellular cytotoxicity and complement-mediated cell lysis. The capacity for B-cell reconstitution and preexisting humoral immunity is preserved [4], such as levels of IgG and IgM antibodies in the blood of cerebrospinal fluid. Ocrelizumab may induce antibody-dependant cellular cytotoxicity involving macrophages, natural killer cells, and cytotoxic T cells that act together to cause cell death [3]. Another mechanism is apoptosis, which may result from cross-linking membrane CD20 on the target cell surface [3].

| | |
|---|---|
| (A) | B-lymphocyte antigen CD20 |
| | antagonist<br>antibody |
| | Human |

### Absorption

Ocrelizumab displays a two-compartment pharmacokinetic model with time-dependent clearance. The overall exposure at the steady-state (AUC over the 24 week dosing intervals) of ocrelizumab was 3,510 mcg/mL per day. Following intravenous infusion of maintenance doses of 600 mg every 6 months in relapsing MS patients, the mean peak plasma concentration (Cmax) was 212 mcg/mL. Following intravenous infusion of two 300 mg doses separated by 14 days every 6 months in patients with PPMS, Cmax was reported to be 141 mcg/mL. The pharmacokinetics of ocrelizumab was essentially linear and dose proportional between 400 mg and 2000 mg [Label].

### Volume of distribution

Central volume of distribution was 2.78 L [Label].

### Protein binding

As with other antibodies, ocrelizumab is expected to undergo nonspecific catabolism and broken into smaller peptides and amino acids [Label].

### Route of elimination

Not Available

### Half life

The terminal elimination half-life was 26 days [Label].

### Clearance

Constant clearance was estimated at 0.17 L/day, and initial time-dependent clearance at 0.05 L/day. Peripheral volume and inter-compartment clearance were estimated at 2.68 L and 0.29 L/day, respectively [Label].

### Toxicity

Studies assessing the carcinogenicity and mutagenicity of ocrelizumab have not been conducted [Label].

### Affected organisms

Humans and other mammals

### Pathways

Not Available

### Pharmacogenomic Effects/ADRs

Not Available

## INTERACTIONS

### Drug Interactions

Search

| DRUG | INTERACTION | DRUG GROUP |
|---|---|---|

| | | |
|---|---|---|
| | activities of Abatacept. | |
| Abetimus | Ocrelizumab may increase the immunosuppressive activities of Abetimus. | Investigational |
| Acteoside | Ocrelizumab may increase the immunosuppressive activities of Acteoside. | Investigational |
| Adalimumab | Ocrelizumab may increase the immunosuppressive activities of Adalimumab. | Approved |
| Adefovir | Ocrelizumab may increase the immunosuppressive activities of Adefovir. | Investigational |
| Afelimomab | Ocrelizumab may increase the immunosuppressive activities of Afelimomab. | Investigational |
| Alefacept | Ocrelizumab may increase the immunosuppressive activities of Alefacept. | Approved, Investigational, Withdrawn |
| Alemtuzumab | Ocrelizumab may increase the immunosuppressive activities of Alemtuzumab. | Approved, Investigational |
| Alicaforsen | Ocrelizumab may increase the immunosuppressive activities of Alicaforsen. | Investigational |

Showing 1 to 10 of 198 entries

‹ ›

## Food Interactions

Not Available

## REFERENCES

### General References


1. McGinley MP, Moss BP, Cohen JA: Safety of monoclonal antibodies for the treatment of multiple sclerosis. Expert Opin Drug Saf. 2017 Jan;16(1):89-100. Epub 2016 Oct 31. [PubMed:27756172]
2. Reddy V, Dahal LN, Cragg MS, Leandro M: Optimising B-cell depletion in autoimmune disease: is obinutuzumab the answer? Drug Discov Today. 2016 Aug;21(8):1330-8. doi: 10.1016/j.drudis.2016.06.009. Epub 2016 Jun 22. [PubMed:27343722]
3. Sorensen PS, Blinkenberg M: The potential role for ocrelizumab in the treatment of multiple sclerosis: current evidence and future prospects. Ther Adv Neurol Disord. 2016 Jan;9(1):44-52. doi: 10.1177/1756285615601933. [PubMed:26788130]

5. FDA Press Announcements: FDA approves new drug to treat multiple sclerosis [Link]

### External Links

KEGG Drug

D05218

PubChem Substance

347911266

Wikipedia

Ocrelizumab

### AHFS Codes

92:20.00 — Immunomodulatory Agents

### FDA label

Download (249 KB)

## CLINICAL TRIALS

### Clinical Trials

Search

| PHASE | STATUS | PURPOSE | CONDITIONS | COUNT |
|---|---|---|---|---|
| 1, 2 | Completed | Treatment | Non-Hodgkin's Lymphoma (NHL) | 1 |
| 1, 2 | Completed | Treatment | Rheumatoid Arthritis | 1 |
| 1, 2 | Terminated | Treatment | Rheumatoid Arthritis | 1 |
| 2 | Active Not Recruiting | Treatment | Relapsing Remitting Multiple Sclerosis (RRMS) | 1 |
| 2 | Terminated | Treatment | Rheumatoid Arthritis | 2 |
| 3 | Active Not Recruiting | Treatment | Multiple Sclerosis, Primary Progressive | 1 |

| | | | | |
|---|---|---|---|---|
| | Recruiting | | | |
| 3 | Active Not Recruiting | Treatment | Rheumatoid Arthritis | 1 |
| 3 | Completed | Treatment | Nephritis, Lupus / Systemic Lupus Erythematosus (SLE) | 1 |

Showing 1 to 10 of 23 entries

‹ ›

## PHARMACOECONOMICS

### Manufacturers

Not Available

### Packagers

Not Available

### Dosage forms

Search

| FORM | ROUTE | STRENGTH |
|---|---|---|
| Injection | Intravenous | 300 mg/10mL |
| Solution | Intravenous | 30 mg |

Showing 1 to 2 of 2 entries

‹ ›

### Prices

Not Available

### Patents

Not Available

## PROPERTIES

Not Available

## TAXONOMY

**Description**

Not Available

**Kingdom**

Organic Compounds

**Super Class**

Organic Acids

**Class**

Carboxylic Acids and Derivatives

**Sub Class**

Amino Acids, Peptides, and Analogues

**Direct Parent**

Peptides

**Alternative Parents**

Not Available

**Substituents**

Not Available

**Molecular Framework**

Not Available

**External Descriptors**

Not Available

## 1. B-lymphocyte antigen CD20

**Kind**

Protein

**Organism**

Human

**Pharmacological action**

Yes

**Actions**

Antagonist Antibody

**General Function**

Mhc class ii protein complex binding

**Specific Function**

This protein may be involved in the regulation of B-cell activation and proliferation.

**Gene Name**

MS4A1

**Uniprot ID**

P11836

**Uniprot Name**

B-lymphocyte antigen CD20

**Molecular Weight**

33076.99 Da

### References


1. McGinley MP, Moss BP, Cohen JA: Safety of monoclonal antibodies for the treatment of multiple sclerosis. Expert Opin Drug Saf. 2017 Jan;16(1):89-100. Epub 2016 Oct 31. [PubMed:27756172]
2. Reddy V, Dahal LN, Cragg MS, Leandro M: Optimising B-cell depletion in autoimmune disease: is obinutuzumab the answer? Drug Discov Today. 2016 Aug;21(8):1330-8. doi: 10.1016/j.drudis.2016.06.009. Epub 2016 Jun 22. [PubMed:27343722]

This project is supported by the **Canadian Institutes of Health Research** (award #111062), **Alberta Innovates - Health Solutions**, and by **The Metabolomics Innovation Centre (TMIC)**, a nationally-funded research and core facility that supports a wide range of cutting-edge metabolomic studies. TMIC is funded by **Genome Alberta**, **Genome British Columbia**, and **Genome Canada**, a not-for-profit organization that is leading Canada's national genomics strategy with funding from the federal government. Maintenance, support, and commercial licensing is provided by **OMx Personal Health Analytics, Inc.** Designed by **Educe Design & Innovation Inc.**