**Overview of the patent status of MS treatments: update on rituximab, ocrelizumab, cladribine and glatiramer acetate**

**Date: 03.11.2022**

Contents

[1. Cladribine [Mavenclad®, EMD Serono/Merck KGaA; US 2019] 1](#_Toc119646459)

[2. Glatiramer acetate [several brand names but innovator was Copaxone®] 1](#_Toc119646460)

[3. Ocrelizumab [Ocrevus®] 2](#_Toc119646461)

[4. Rituximab [several brand names, Rituxan®] 3](#_Toc119646462)

### Cladribine [Mavenclad®, EMD Serono/Merck KGaA; US 2019]

**Cladribine** compound patents expired in 2005. Patents on the oral formulation of cladribine with cyclodextrin have been granted in several countries including Brazil, India, China, South Africa, EP and US. Patents originally expiring in 2024 have been extended by way of Supplementary Protection Certificates in Europe until 2029 (e.g., in Estonia, Slovakia, Romania, Lithuania, Luxembourg, Poland, Latvia, Slovenia, Albania, Bulgaria, Cyprus and Greece). Patent applications on cladribine treatment regimen for MS with an expected expiry in 2025 were filed in several countries and granted e.g. in Brazil, China, Russia, Ukraine, South Africa, US and EP. In India the equivalent application was abandoned.

A US patent owned by Merck KGaA covering a method of treating a progressive form of Multiple Sclerosis was recently granted and added to the USFDA orange book. Equivalents are pending in several countries and the expected expiry is 10.09.2041.

*Patent landscape for cladribine.*

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| **Description** | **Applicant** | **International publication** | **Expected date of expiry in LMICs** | **ARIPO** | **BRA** | **CHN** | **EAPO** | **GTM** | **IDN** | **IND** | **MAR** | **OAPI** | **PHL** | **THA** | **UKR** | **ZA** | **VNM** | **US** | **EP** |
| Cladribine product | Brigham Young University | [US4760137](https://worldwide.espacenet.com/publicationDetails/biblio?DB=EPODOC&II=0&ND=3&adjacent=true&locale=en_EP&FT=D&date=19880726&CC=US&NR=4760137A&KC=A) | 26.07.2005 |  |  |  |  |  |  |  |  |  |  |  |  |  |  | N | N |
| Oral formulation of cladribine (with cyclodextrin) | Ares Trading SA (Ivax Corporation) | [WO2004087101](https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2004087101&redirectedID=true) | 26.03.2024 | . | G | G | G | . | . | G | . | . | . | . | . | G | . | G | G #29 |
| Treatment regimen for MS with cladribine-free periods | Serono Laboratories SA | [WO2006067141](https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2006067141&_cid=P20-L81GFO-20468-1) | 20.12.2025 | . | G | G | G\* | . |  | N | . | . |  |  | G | G | . | G  26 | G |
| Cladribine regimen for use in treating progressive forms of multiple sclerosis | Merck Patent GmbH | [WO2019101960](https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2019101960&_cid=P20-L81BNN-45207-1) | 23.11.2038 | . | F | F | F | . | F | F | N | . | . | . | . | F | . | G | F |

### Glatiramer acetate [several brand names but innovator was Copaxone®]

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The patents on **glatiramer acetate** filed in 1994 by Yeda Research and Development Co., Ltd have expired in 2015. In the LMIC jurisdictions surveyed, secondary patents expected to expire in 2030 and relating to a specific treatment regimen of RRMS with glatiramer acetate have been granted in EAPO, and Ukraine and have been rejected in Brazil, China and India. The equivalent patents in the USA have not prevented the entry of generic versions of **glatiramer acetate** which are also available in other countries.

*Patent landscape for glatiramer acetate.*

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| Product, compositions and manufacturing process | Yeda R&D Co Ltd | [WO1995031990](https://patentscope.wipo.int/search/en/detail.jsf?docId=WO1995031990&_cid=P12-L9GYRM-51336-1) | 2014-2015 | . | N | N | N | . | N | . | . | . |  | . | N | N | . | N | N |
| Glatiramer acetate use in delaying the onset of clinically definite multiple sclerosis | Yeda R&D Co Ltd | [WO2009070298](https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2009070298&_cid=P10-LA19AT-34324-1) | 26.11.2028 |  | N | N | N |  |  |  |  |  |  |  |  |  |  | N | N |
| Treatment regimen of RRMS with glatiramer Acetate | Yeda R&D Co Ltd | [WO2011022063](https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2011022063&_cid=P12-L9GYSM-51843-1) | 19.08.2030 | . | N | N | G | . | F/C | . | . | . |  | . | G | G | . | G | G |

### Ocrelizumab [Ocrevus®]

**Ocrelizumab** is protected by a product patent expiring in 2023 in many jurisdictions (sometimes extended by way of patent term extensions or supplementary protection certificates until 2028 or 2029). It has generally been filed or granted in the countries/regions surveyed except in ARIPO, OAPI, and Guatemala. It is likely that biosimilar ocrelizumab cannot enter the market where this patent has been granted, before 2023. A secondary patent family, expiring 2029, is granted in China, EAPO, Philippines and South Africa, refused in Brazil, pending in Thailand, and has not been filed in other LMIC jurisdictions that were surveyed. The secondary patent family expiring 2035/36 was filed in few High-Income Jurisdictions and refused in China.

Regarding the secondary patents on ocrelizumab (expiring 2029, possibly as late as 2036) further consultation would be necessary to establish whether these represent a true block to generic market entry. This may depend on the practical enforceability of method-of-use patents in each jurisdiction.

*Patent landscape for ocrelizumab.*

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| **Description** | **Applicant** | **International publication** | **Expected date of expiry in LMICs** | **ARIPO** | **BRA** | **CHN** | **EAPO** | **GTM** | **IDN** | **IND** | **MAR** | **OAPI** | **PHL** | **THA** | **UKR** | **ZA** | **VNM** | **US** | **EP** |
| Product patent | Genentech; Roche | [WO2004056312 WO2004060052 WO2004060053](https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2004056312&_cid=P22-L8TYJL-13232-1) | 16.12.2023 | . | G | G | G\* RU BY | . | G | G | G | . | G | G | G | G | G | G #25  -28 | G  #28-29 |
| Method of use in MS - progressive multiple sclerosis | Genentech; Roche | [WO2010033587](https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2010033587&_cid=P22-L8TYLD-13944-1) | 16.09.2029 | . | N | G | G | . | . | N | . | . | G | F | . | G | . | G | G |
| Method of use in MS - Improving functional ability in a patient with MS - (MPP search) | Genentech; Roche | [WO2017062682](https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2017062682&redirectedID=true) | 06.10.2036 | . | . | N | . | . | . | . | . | . | . | . | . | . | . | F | F |

### Rituximab [several brand names, Rituxan®]

**Rituximab** product patents expired between 2015 and 2018. Biosimilar versions of **rituximab** have been approved in numerous countries, including, for example, the European Union, South Korea, Bolivia, Chile, Peru, India, and Australia[[1]](#footnote-1). Secondary method of use patents concerning rituximab have been filed or granted in some jurisdictions, including in China, Malaysia, Mexico, and South Africa. Many have expired between 2018 and 2020 and two patent families covering the use of rituximab to treat rheumatoid arthritis and joint damage are expected to expire in 2024 and 2026 respectively. Apart from these, there do not appear to be active patents covering the intravenous formulation of rituximab.

Secondary formulation patents for a subcutaneous administration form of rituximab (rituximab and hyaluronidase human approved to Genentech in the USA as RITUXAN HYCELA™) have been granted in the majority of LMIC jurisdictions that were surveyed including Brazil, China, Morocco, Ukraine, south Africa and Vietnam (expected to expire in **2030**). The equivalent Indian application was refused in October 2022.

In 2005 Genentech filed an international application of a specific treatment regimen of rituximab in MS however patents have been refused in many jurisdictions in view of the prior art created by the Genmab’s international patent on ofatumumab and its uses, including in MS (WO2004035607). Patents have been granted in Russia, Philippines and South Africa with an expected expiry in 2025.

*Patent landscape for rituximab (not all expired patents listed)*

| **Description** | **Applicant** | **International publication** | **Expected date of expiry in LMICs** | **ARIPO** | **BRA** | **CHN** | **EAPO** | **GTM** | **IDN** | **IND** | **MAR** | **OAPI** | **PHL** | **THA** | **UKR** | **ZA** | **VNM** | **US** | **EP** |
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| Rituximab therapy (product & use) | IDEC pharmaceuticals | [WO1994011026](https://patentscope.wipo.int/search/en/detail.jsf?docId=WO1994011026&_cid=P10-L0KRDZ-38018-1) | 12.11.2013 | . | N | N | N | u | N | . | u | u | G #22 | N | u | N | N | G  19-22 | G #18 |
| Use of rituximab to treat Rheumatoid Arthritis in a patient with an inadequate response to a tnf-alpha inhibitor | Genentech | [WO2004091657](https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2004091657&_cid=P11-L2T1E2-82870-1) | 06.04.2024 | . | N | N | N\* | . | G | G | G | . | G | . | G | G | G | G | N |
| Method for treating joint damage | Roche; Biogen; IDEC pharmaceuticals | [WO2007059188](https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2007059188&_cid=P10-LA1B9P-64341-1) | 14.12.2026 | . | N | N | . | . | N | N | G | . | G | F | G | G | F | G | N |
| Formulation for subcutaneous injection (comprises hyaluronidase enzyme) | Roche | [WO2011029892](https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2011029892&_cid=P11-L2YN7I-50574-1) | 10.09.2030 | . | G | G | G | F | F | N | N | . | G | G | G | G | G | G | G |
| Method for treating MS with a CD20 antibody (specific regimen) - (MPP search) | Genentech | [WO2005117978 (Genentech)](https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2005117978&_cid=P22-L0KRYC-95809-1) | 02.06.2025 | . | N | N | G\* | F | F | N | . | . | G | F | . | G | . | N | N |

Note:

The information above is provided for educational purposes only and does not constitute legal advice. This report provides a snapshot at a point in time and may not be comprehensive.

Various types of patents may be granted for pharmaceuticals. In general, a patent covering the specific active molecule (a ‘product patent’) is considered ‘strongest’, that is, most likely to prevent generic products from entering the market. Other types of patents, sometimes termed ‘secondary’ patents, can cover aspects such as method of use, specific formulations (e.g. formulation as a tablet with specific excipients) or production methods.

The main patents and patent applications relating to products were identified thanks to the [US FDA Orange Book](https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm) and [Health Canada Patent Register](https://pr-rdb.hc-sc.gc.ca/pr-rdb/index-eng.jsp) databases. Both regulatory agencies list patents relevant to approved medicines that are provided by market authorization holders. The Canadian and/or US patents retrieved are used to identify equivalent patents/patent applications in other jurisdictions using regional or national patent office public databases. For “old” products, if there are basically no “unexpired” patents left in Canada and US, one can be reasonably certain (though not absolutely sure) that it is unlikely there will be in other countries.

It should be noted that the patent information provided herein may not be comprehensive and further analysis required to identify patents directed to categories excluded from the US FDA Orange Book or Health Canada Patent Register (e.g. manufacturing processes) or patent applications that have not yet been made public for more recent innovations.

While in general it is safe to assume that an unexpired product patent, where it is granted and in force, will block generic entry, whether secondary patents block generic market entry is a more difficult question. In many cases, generic manufacturers can ‘invent around’ secondary patents to avoid infringement.

The patent searches were limited to a few sample countries, including countries where several leading generic manufacturers are located (e.g. Brazil, China, India, South Africa, Thailand), relevant regional patent offices (ARIPO, EAPO and OAPI) and an illustrative sample of Low middle Income Countries (LMICs) from other regions (e.g. Guatemala, Indonesia, Morocco, Ukraine and Vietnam).

**Patent Status / Acronyms and abbreviations**

G granted

F filed/pending

N not in force (abandoned, expired, withdrawn, invalidated)

. not filed

u Status unknown

\* No EAPO filing but national filing in Russia (RU)

# expiry dates depending of patent term extension granted

**Countries/Regional patent organisations**

ARIPO African Regional Intellectual Property Organization (19 states)

BRA Brazil

CHN China

EAPO Eurasian Patent Organization (8 states including Russia)

EPO/EP European Patent Organization (covers most of European countries). In addition, European patents can for example be validated in Morocco if filed on or after 1 March 2015, in Tunisia if filed on or after 1 December 2017 and Cambodia if filed on or after 1 March 2018.

GTM Guatemala

IDN Indonesia

IND India

MAR Morocco

OAPI Organisation Africaine de la Propriété Intellectuelle (17 states)

PHL Philippines

THA Thailand

UKR Ukraine

US Unite States of America

VNM Vietnam

ZAF South Africa

1. Generics and Biosimilars Initiative. Biosimilars of rituximab. http://www.gabionline.net/Biosimilars/General/Biosimilars-of-rituximab [↑](#footnote-ref-1)