Ocrevus® (*ocrelizumab*)

Clinical summary

Disease characteristics

- Multiple sclerosis (MS) is an immune-mediated inflammatory demyelinating disease of the central nervous system. Major clinical types include:
    - **Relapsing MS (RMS):**
        - **Relapsing-remitting multiple sclerosis (RRMS)** – RRMS is characterized by clearly defined relapses with either full recovery, or with sequelae and residual deficit upon recovery. There is minimal or no disease progression between relapses, though individual relapses may result in severe residual disability.
        - **Secondary progressive multiple sclerosis (SPMS)** - SPMS begins as relapsing-remitting disease, hence the designation of "secondary," but over time the disease enters a stage of steady deterioration in function, with or without superimposed attacks. Secondary progressive disease is the single largest category of MS. Typically, when the secondary progressive stage is reached, the relapse rate is also reduced. This type of MS, which ultimately develops in as many as 90% of patients with RRMS after 25 years, causes the greatest amount of neurologic disability attributable to MS. [1]
    - **Primary progressive multiple sclerosis (PPMS)** - PPMS represents approximately 10% of MS cases and is characterized by disease progression from onset. However, occasional plateaus, temporary minor improvements, and acute relapses may occur. [2]

Drug therapy[3]

Adult patients

- The disease-modifying therapies (DMT) currently approved for use in the US include:[4]
    - Interferons (e.g., IFN beta-1a, IFN beta-1b, peginterferon beta-1a)
    - Sphingosine 1-phosphate (S1P) receptor modulators (fingolimod, ozanimod, ponesimod, siponimod)

[1] Initial disease-modifying therapy for relapsing-remitting multiple sclerosis in adults. UpToDate. June 2026. Accessed 7/14/2026
[2]Treatment of Primary Progressive Multiple Sclerosis in Adults. UpToDate. June 2026. Accessed 7/23/2026
[3] This discussion is limited to the monoclonal antibodies as those are the therapeutic alternatives selected for review by the Board. This is not a complete review of all DMTs and considerations for treatment.
[4] Multiple Sclerosis Treatment & Management. Medscape. (Accessed July 22, 2026.)

    - Monoclonal antibodies (alemtuzumab, natalizumab, ocrelizumab, ofatumumab, ublituximab)
    - Miscellaneous immunomodulators (cladribine, dimethyl fumarate, glatiramer, mitoxantrone, teriflunomide)
  - Most of the disease-modifying agents have been approved for use only in relapsing forms of MS. However, cladribine, ocrelizumab, ozanimod, ponesimod, and siponimod are also approved for active secondary progressive disease.
- The monoclonal antibody rituximab is widely used off label to treat RRMS and SPMS; there are limited but convincing data from randomized controlled trials.[5]
    - ICER recommends that payers should remove barriers to rituximab use, especially biosimilar rituximab, for RMS patients who are appropriate candidates for the therapy. Payers should not unilaterally implement policies to switch RMS patients who are stable on their DMT to lower-cost biosimilar rituximab.[6]
- Generally, published guidelines do not indicate a preference for a specific DMT in RRMS treatment, instead emphasizing the importance of shared decision making based on patient preferences and factors that include safety, route of administration, lifestyle, cost, efficacy, common adverse events and tolerability.[7,8]
- For patients with PPMS who are younger (age $\leq$ 55 years) and/or have active disease on MRI and no contraindications, ocrelizumab is recommended unless the risks of treatment outweigh the benefits.[8,9] For patients with PPMS who are older and without disease activity, symptomatic therapy may be most appropriate.[10]
- For patients with active SPMS, it is suggested that clinicians use a DMT, with the choice individualized based upon disease activity and progression, adverse effect profile, and patient preference. Potential therapeutic options for patients with active SPMS for patients in the US include all DMTs approved for relapsing forms of MS.[11]

Pediatric patients

- Pediatric Onset MS (POMS), defined as the onset of MS occurring before the age of 18, is less common than adult-onset MS and accounts for approximately 5% of cases. The

[5] Olek MJ, Mowry EM. Clinical use of monoclonal antibody disease-modifying therapies for multiple sclerosis. In: UpToDate, Wolters Kluwer. (Accessed July 24, 2026.)
[6] Oral and Monoclonal Antibody Treatments for Relapsing Forms of Multiple Sclerosis: Effectiveness and Value Final Evidence Report. Institute for Clinical and Economic Review. February 21, 2023. https://icer.org/wp-content/uploads/2022/04/ICER_MS_Final_Evidence_Report_022123.pdf Accessed 7/12/2026
[7] Practice guideline: Disease-modifying therapies for adults with multiple sclerosis. April 24, 2018. https://www.neurology.org/doi/full/10.1212/WNL.0000000000005347#sec-1 . Accessed 7/14/2026
[8] Olek MJ, Mowry EM. Initial disease-modifying therapy for relapsing-remitting multiple sclerosis in adults. In: UpToDate. Wolters Kluwer.(Accessed July 14, 2026.)
[9] Olek MJ, Mowry EM. Treatment of Primary Progressive Multiple Sclerosis in Adults. In: UpToDate. Wolters Kluwer. (Accessed July 23, 2026.)
[10] Ibid
[11] Olek MJ, Mowry EM. Treatment of Secondary Progressive Multiple Sclerosis in Adults. UpToDate. In: UpToDate, Wolters Kluwer. (Accessed July 23, 2026.).

disease is not well studied in children and guidelines have not been updated recently, either internationally or in the U.S.; the most recent U.S. guidelines for pediatric patients were updated in 2011.

- Because of the absence of specific and standardized guidelines for managing POMS and the lack of randomized clinical trials, treatment strategies often depend on the clinical expertise of neurologists, who frequently adapt MS therapeutic protocols developed for adults.
- Pediatric management is similar to that for adults; treatment with a DMT is recommended for children who develop RRMS.
- As discussed in UpToDate, a peer-reviewed, continuously updated clinical decision support resource used by health care professionals to guide evidence-based practice, the preferred approach is to use a high or intermediate efficacy DMT, such as rituximab, fingolimod, or dimethyl fumarate. There is evidence that these DMTs are more effective than the older injectable DMTs (interferons and glatiramer) for reducing the relapse rate and the accumulation of new brain lesions, but they also have a higher rate of serious adverse events.
- Aside from Ocrevus, fingolimod is the only other FDA-approved drug (in 2018) for the treatment of POMS (in ages 10 and up); pediatric trials present specific challenges in this population. Older agents are often preferred since injections are limited to weekly or biweekly; however, the weekly interferon beta-1a (Avonex) therapy may be less well tolerated in some patients. Initial choice is again influenced by patient and family preferences and must include shared decision making.[12,13,14,15]

Clinical comparison: Monoclonal antibody therapies

Table 1 Clinical comparison of the review drug and its therapeutic alternatives

Drug	Formulation	RMS	PPMS	Pediatric RMS	Expected Biosimilar Availability
Ocrevus (ocrelizumab)	IV infusion	FDA Approved	FDA Approved	FDA Approved	~March 2029

[12] Lotze TM. Treatment and Prognosis of Pediatric Multiple Sclerosis. In: UpToDate, Wolters Kluwer. (Accessed July 28, 2026.)

[13] Management of Pediatric Central Nervous System Demyelinating Disorders: Consensus of United States Neurologists. Journal of Child Neurology. April 25, 2011.

[14] Pediatric Multiple Sclerosis: A Systematic Exploration of Effectiveness in Current and Emerging Therapeutics. Pediatric Neurology. July 2025. https://www.sciencedirect.com/science/article/abs/pii/S0887899425000906 Accessed 7/28/26

[15] Current and Emerging Treatment Options in Pediatric Onset Multiple Sclerosis. Sclerosis. April 1, 2024. https://doi.org/10.3390/sclerosis2020007 Accessed 7/28/2026

Drug	Formulation	RMS	PPMS	Pediatric RMS	Expected Biosimilar Availability
Briumvi (ublituximab-xiiy)	IV infusion	FDA Approved	-	-	2042
Kesimpta (ofatumumab)	SC pen/syringe	FDA Approved	-	-	~2030
Lemtrada (alemtuzumab)	IV infusion	FDA Approved	-	-	None appear to be in development
Rituxan (rituximab)	IV infusion	Off label use	-	Off label use	Ruxience, Riabni, Truxima, available 2019
Tysabri (natalizumab)	IV infusion	FDA Approved	-	-	Tyruko, available 2025

Additional information on the drug and therapeutic equivalents is included in the appendix.

Appendix A: Clinical information

Drug indications[16]

- FDA Approved:
  - Ocrevus is a CD20-directed cytolytic antibody indicated for the treatment of:
    - **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
    - **Relapsing-remitting MS, in pediatric patients** 10 years of age and older who weigh 25 kg or more

Clinical efficacy

Efficacy in relapsing forms of MS in adults

The efficacy of Ocrevus was demonstrated in two randomized, double-blind, double-dummy, active comparator-controlled clinical trials of identical design, in adult patients with relapsing forms of multiple sclerosis (RMS) treated for 96 weeks (Study 1 and Study 2). The dose of Ocrevus was 600 mg every 24 weeks (initial treatment was given as two 300 mg IV infusions administered 2 weeks apart, and subsequent doses were administered as a single 600 mg IV infusion) and the dose of Rebif (interferon beta-1a), the active comparator, was 44 mcg given as subcutaneous injections 3 times per week. The primary outcome of both Study 1 and Study 2 was the annualized relapse rate (ARR). Ocrevus significantly lowered the annualized relapse rate and the proportion of patients with disability progression confirmed at 12 weeks after onset compared to Rebif.

Table 2 Clinical efficacy in relapsing MS

	Study 1		Study 2	
	Ocrevus	**Rebif**	**Ocrevus**	**Rebif**
Clinical Endpoints	**N=410**	**N=411**	**N=417**	**N=418**
Annualized Relapse Rate	0.156	0.292	0.155	0.290
Relative Reduction	46% (p<0.0001)		47% (p<0.0001)	

Efficacy in primary progressive MS in adults

Study 3 was a randomized, double-blind, placebo-controlled clinical trial in patients with primary progressive multiple sclerosis (PPMS). Patients were randomized 2:1 to receive either Ocrevus 600 mg or placebo as two 300 mg intravenous infusions 2 weeks apart every 24 weeks

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

for at least 120 weeks. The primary outcome was the time to onset of disability progression attributable to MS confirmed to be present at the next neurological assessment at least 12 weeks later. The time to onset of disability progression confirmed at 12 weeks after onset was significantly longer for Ocrevus-treated patients than for placebo-treated patients.

Table 3 Clinical efficacy in primary progressive MS

	Study 3	
	Ocrevus	**Placebo**
Clinical Outcomes	**N=488**	**N=244**
Proportion of patients with 12-week confirmed disability progression*	32.90%	39.30%
Risk reduction	24%; p=0.0321	
*Defined as an increase of 1.0 point or more from the baseline EDSS score for patients with baseline score of 5.5 or less, or an increase of 0.5 or more when the baseline score is more than 5.5		

Efficacy in relapsing-remitting MS in pediatric patients 10 years to less than 18 years of age

The efficacy and safety of Ocrevus in pediatric patients 10 years to less than 18 years of age with RRMS was established in a randomized, double-blind, double-dummy clinical study with a follow-up time of at least 24 weeks. Patients were randomized 1:1 to receive either Ocrevus intravenously according to the recommended dosage regimen or 0.5 mg fingolimod daily by mouth. The primary outcome was ARR. Ocrevus demonstrated non-inferiority to fingolimod in reducing the ARR and superiority in reducing the annualized rate of new/enlarging T2 lesions during the double-blind period and reducing the number of Gd-enhancing T1 lesions at Week 12.[17]

Table 4 Clinical efficacy in pediatric RRMS

	Study 5	
	Ocrevus	**Fingolimod**
Clinical Endpoints	**N=93**	**N=94**
Annualized relapse rate	0.07	0.135
Relative reduction	48.30%	

[17] A Study to Evaluate Safety and Efficacy of Ocrelizumab in Comparison With Fingolimod in Children and Adolescents With Relapsing-remitting Multiple Sclerosis (RRMS) (Operetta 2). (n.d.). Retrieved from https://clinicaltrials.gov/study/NCT05123703?term=NCT05123703+&viewType=Card&rank=1

Clinical safety

- FDA safety warnings and precautions for Ocrevus:
  - Infusion reactions
  - Infections: Serious, including life-threatening and fatal infections, have occurred.
  - Progressive multifocal leukoencephalopathy (PML)
  - Reduction in immunoglobulins
  - Malignancies: An increased risk of malignancy, including breast cancer, may exist with Ocrevus.
  - Immune-Mediated Colitis: Immune-mediated colitis has been reported in the postmarketing setting.
  - Liver Injury: Clinically significant liver injury has occurred.
- Contraindications:
  - Active hepatitis B virus infection
  - History of life-threatening infusion reaction to Ocrevus
- Common side effects:
  - RMS (incidence ≥10% and > REBIF®): upper respiratory tract infections and infusion reactions
  - PPMS (incidence ≥10% and > placebo): upper respiratory tract infections, infusion reactions, skin infections, and lower respiratory tract infections
  - RRMS in pediatric patients 10 years of age and older: Adverse reactions were consistent with those observed in adults with RMS

Therapeutic alternatives

Table 5 FDA approved indications

Drug	RMS	PPMS	Pediatric RMS
Ocrevus (ocrelizumab)	Yes	Yes	Yes
Briumvi (ublituximab-xiiy)[18]	Yes	-	-
Kesimpta (ofatumumab)[19]	Yes	-	-
Lemtrada (alemtuzumab)[a] [20]	Yes[b]	-	-
Rituxan (rituximab)[c] [21]	-	-	-

[18] U.S. Food & Drug Administration. *Briumvi (ublituximab) Prescribing Information*. TG Therapeutics, Revised 01/2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/761238s026lbl.pdf
[19] U.S. Food & Drug Administration. *Kesimpta (ofatumumab) Prescribing Information*. Novartis, Revised 04/2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/125326s084lbl.pdf
[20] U.S. Food & Drug Administration. *Lemtrada (alemtuzumab) Prescribing Information*. Genzyme, Revised 05/2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/103948s5193lbl.pdf
[21] U.S. Food & Drug Administration. *Rituxan (rituximab) Prescribing Information*. Genentech, Revised 12/2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/103705s5467lbl.pdf

Drug	RMS	PPMS	Pediatric RMS
Tysabri (natalizumab)[22]	Yes	-	-

[a] Because of its safety profile, the use of Lemtrada should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.
[b] Lemtrada is not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile.
[c] Rituxan is not FDA-approved for any MS indications. Use in MS is off-label.

Table 6 Summary of key clinical trials - RMS[23]

	Treatment drug	Population	Annualized relapse Rate	Relative reduction
Ocrevus Study 1	**Ocrevus**	N=410	0.156	46% (p<0.0001)
	Rebif	N=411	0.292	
Ocrevus Study 2	**Ocrevus**	N=417	0.155	47% (p<0.0001)
	Rebif	N=418	0.29	
Briumvi Study 1[24]	**Briumvi**	N=271	0.076	59% (p<0.001)
	Teriflunomide	N=274	0.188	
Briumvi Study 2[25]	**Briumvi**	N=272	0.091	49% (p = 0.002)
	Teriflunomide	N=272	0.178	
Kesimpta Study 1[26]	**Kesimpta**	N=465	0.11	51% (p < 0.001)
	Teriflunomide	N=462	0.22	
Kesimpta Study 2[27]	**Kesimpta**	N=481	0.10	58% (p < 0.001)
	Teriflunomide	N=474	0.25	
Lemtrada Study 1	**Lemtrada**	N=426	0.26	49% (p <0.0001)
	Rebif	N=202	0.52	

[22] U.S. Food & Drug Administration. *Tysabri (natalizumab) Prescribing Information*. Biogen, Revised 03/2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/103705s5467lbl.pdf
[23] Data are presented from separate pivotal trials for each agent. Trials are not direct head-to-head comparative trials; differences in trial design, patient population, and follow-up duration preclude direct statistical comparison of the results shown.
[24] Study to Assess the Efficacy and Safety of Ublituximab in Participants With Relapsing Forms of Multiple Sclerosis (RMS) (ULTIMATE 1). Retrieved from https://clinicaltrials.gov/study/NCT03277261?term=NCT03277261&viewType=Card&rank=1
[25] Study to Assess the Efficacy and Safety of Ublituximab in Participants With Relapsing Forms of Multiple Sclerosis (RMS) (ULTIMATE II). Retrieved from https://clinicaltrials.gov/study/NCT03277248?term=NCT03277248&viewType=Card&rank=1
[26] Efficacy and Safety of Ofatumumab Compared to Teriflunomide in Patients With Relapsing Multiple Sclerosis (ASCLEPIOS I). Retrieved from https://clinicaltrials.gov/study/NCT02792218?term=NCT02792218&viewType=Card&rank=1
[27] Efficacy and Safety of Ofatumumab Compared to Teriflunomide in Patients With Relapsing Multiple Sclerosis. (ASCLEPIOS II). Retrieved from https://clinicaltrials.gov/study/NCT02792231?term=NCT02792231&viewType=Card&rank=1

Lemtrada Study 2	**Lemtrada**	N=347	0.18	55% (p <0.0001)
	Rebif	N=187	0.39	
Tysabri Study 1	**Tysabri**	N=627	0.22	67% (p <0.0001)
	Placebo	N=315	0.67	
Tysabri Study 2	**Tysabri + Avonex**	N=589	0.33	56% (p <0.0001)
	Placebo + Avonex	N=582	0.75	

Table 7 Strengths, adult dosing and route

Drug	Formulation	Initial dose	Maintenance dose
Ocrevus (ocrelizumab)	IV infusion	300 mg at weeks 0 and 2	600 mg every 6 months
Briumvi (ublituximab-xiiy)	IV infusion	150 mg at week 0, 450 mg at week 2	450 mg every 24 weeks
Kesimpta (ofatumumab)	SC pen/syringe	20 mg at weeks 0, 1, and 2	20 mg monthly
Lemtrada (alemtuzumab)	IV infusion	12 mg/day for 5 consecutive days,	12 mg/day for 3 consecutive days at least 12 months after the last dose
Rituxan (rituximab)	IV infusion	No FDA-recommended dosing regimen for MS	
Tysabri (natalizumab)	IV infusion	-	300 mg every 4 weeks

Ocrevus dosing in pediatric patients 10 years of age and older includes an initial dose of 150 mg or 300 mg (based on body weight), followed by a second dose two weeks later. Maintenance dosing is 300 mg or 600 mg every 6 months.

Literature describes pediatric rituximab intravenous dosing of 750 mg/m² per dose (max 1000 mg/dose): induction as two doses 14 days apart (or an alternative four-dose induction of 325 mg/m² every 7 days), followed by a single maintenance dose of 750 mg/m² every 6 months.[28]

[28] Lotze TM. Treatment and Prognosis of Pediatric Multiple Sclerosis. In: UpToDate, Wolters Kluwer. (Accessed July 28, 2026.)

Table 8 Selected safety and therapeutic considerations[29]

Drug	Infusion reactions/ hyper-sensitivity	Infections	PML	Reduction in Immuno-globulins	Malignancies	Immune-mediated colitis	Liver injury	Fetal risk
Ocrevus (ocrelizumab)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	-
Briumvi (ublituximab-xiiy)	Yes	Yes	-	Yes	-	-	Yes	Yes
Kesimpta (ofatumumab)	Yes	Yes	-	Yes	-	-	Yes	Yes
Lemtrada (alemtuzumab)	Yes	Yes	Yes	-	Yes	Yes	-	-
Rituxan (rituximab)	-	Yes	-	-	-	-	-	Yes
Tysabri (natalizumab)	Yes	Yes	-	-	-	-	Yes	-

PML = Progressive Multifocal Leukoencephalopathy
Lemtrada includes a Boxed Warning of autoimmunity, infusion reactions, stroke and malignancies. It is available only through a restricted distribution program.
Tysabri includes a Boxed Warning of PML. It is available only through a restricted distribution program.

Clinical benefits and disadvantages

The considerations below reflect guideline- and label-level information for the six board-selected therapeutic alternatives only. Consistent with the limitation noted for the trial data elsewhere in this document, these benefits and disadvantages are not derived from head-to-head efficacy comparisons and should not be read as implying one agent is more effective than another. All six agents fall within the classes generally considered among the higher-effectiveness options for relapsing MS, with the meaningful differences between them centered on route/frequency of administration, monitoring burden, and safety-driven restrictions on use.

Table 9 Review of drug and its therapeutic alternatives: clinical benefits and disadvantages

Drug	Clinical benefits	Clinical disadvantages
Ocrevus (ocrelizumab)	Broadest approved scope among the six agents — the only one	Requires IV infusion with premedication (corticosteroid,

[29] "Yes" indicates the inclusion in the Warnings and Precautions section of the drug's package insert. A dash indicates the consideration was not included in this section. This is not an exhaustive list of safety concerns or adverse reactions.

Drug	Clinical benefits	Clinical disadvantages
	FDA-approved for RMS, PPMS, and pediatric RRMS. Twice-yearly maintenance dosing after initial loading may support long-term adherence.	antihistamine, ± antipyretic) and post-infusion monitoring of at least 1 hour. Precautions include serious infection, PML, malignancy, reduced immunoglobulins, and liver injury.
Briumvi (ublituximab-xiiy)	FDA-approved for RMS with infrequent (every-24-week) maintenance dosing after initial loading.	Two-part IV loading regimen with infusion-reaction risk. Not approved for PPMS or pediatric use. Biosimilar entry is not anticipated until 2042, the latest projected timeline among the six agents.
Kesimpta (ofatumumab)	The only agent among the six administered by self-injected subcutaneous pen, avoiding infusion-center visits.	Monthly maintenance dosing — more frequent than the IV agents reviewed. Not approved for PPMS or pediatric use.
Lemtrada (alemtuzumab)	Defined, time-limited dosing course (two annual treatment cycles) rather than indefinite chronic dosing.	Guideline-reserved for patients with inadequate response to two or more prior MS therapies, due to its safety profile. Boxed warning for autoimmunity, infusion reactions, stroke, and malignancy; available only through a restricted distribution program. Not approved for PPMS or pediatric use. No biosimilar currently appears to be in development.
Rituxan (rituximab)	ICER recommends payers remove barriers to biosimilar rituximab access for appropriate RMS candidates, reflecting a favorable cost position among the B-cell-depleting agents.	No FDA-approved indication or dosing regimen for MS; use is entirely off-label, with dosing individualized by the prescriber.
Tysabri (natalizumab)	Long-standing clinical experience among the monoclonal antibody DMTs.	PML risk requires JCV antibody index assessment before and during use; available only

Drug	Clinical benefits	Clinical disadvantages
		through a restricted distribution program (TOUCH Prescribing Program). Not approved for PPMS or pediatric use.