Healthcare Administered Multiple Sclerosis Medical Drug Criteria Program Summary

The following agents are covered under the medical benefit: Briumvi, Lemtrada, Ocrevus, Tysabri
The following agents are covered under the medical and pharmacy benefit: Ocrevus Zunovo

Multiple Sclerosis

- Preferred agents are: Avonex, Betaseron, dimethyl fumarate, fingolimod, glatiramer, Glatopa, Kesimpta, Mavenclad, Mayzent, Plegridy, Rebif, teriflunomide , Vumerity, Zeposia
- Non-preferred agents are: Aubagio, Bafiertam, Copaxone, Extavia, Gilenya, Ponvory, Tascenso ODT, Tecfidera

Crohn's Disease

- Preferred agents are: Adalimumab-aaty, Adalimumab-adaz, Hadlima, Selarsdi, Simlandi, Skyrizi, Steqeyma, Yesintek

POLICY REVIEW CYCLE

Effective Date **Date of Origin**
07-01-2025

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Briumvi® (ublituximab-xiiy) Injection for intravenous use	Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults		19
Lemtrada® (alemtuzumab) Injection for intravenous use	Treatment of relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease, in adults 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. Limitations of Use: Lemtrada is not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile.		1
Ocrevus® (ocrelizumab) Injection for intravenous use	Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults Treatment of primary progressive MS, in adults		2

Agent(s)	FDA Indication(s)	Notes	Ref#
Ocrevus Zunovo™ (ocrelizumab-hyaluronidase) Injection for subcutaneous use	Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults Treatment of primary progressive MS, in adults		21
Tysabri® (natalizumab) Injection for intravenous use	Monotherapy for the treatment of relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Tysabri increases the risk of progressive multifocal leukoencephalopathy (PML). When initiating and continuing treatment with Tysabri, physicians should consider whether the expected benefit of Tysabri is sufficient to offset this risk. Inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn's disease (CD) with evidence of inflammation who have had an inadequate response to, or are unable to tolerate conventional CD therapies and inhibitors of TNF-alpha Limitations of Use: In CD, Tysabri should not be used in combination with immunosuppressants or inhibitors of TNF-alpha.		3

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Multiple Sclerosis	Multiple sclerosis (MS) is a disorder of the central nervous system (CNS) characterized by demyelization, inflammation, and degenerative changes. Most people with MS experience relapses and remissions of neurological symptoms, particularly early in the disease, and clinical events are usually associated with areas of CNS inflammation. Gradual worsening or progression, with or without subsequent acute attacks of inflammation or radiological activity, may take place early, but usually becomes more prominent over time. While traditionally viewed as a disease solely of CNS white matter, more advanced imaging techniques have demonstrated significant early and ongoing CNS gray matter damage as well.(4) Those diagnosed with MS may have many fluctuating and disabling symptoms (including, but not limited to, fatigue, pain, bladder and bowel issues, sexual dysfunction, movement and coordination problems, visual disturbances, and cognition and emotional changes).(17) There are currently four major types of MS: clinically isolated syndrome (CIS), relapsing-remitting MS (RRMS), primary progressive MS (PPMS), and secondary progressive MS (SPMS).(11)
Relapsing remitting multiple sclerosis (RRMS)	RRMS is characterized by clearly defined attacks (relapses) of new or increasing neurologic symptoms. These relapses are followed by periods of partial or complete recovery. There is no or minimal disease progression during the periods between disease relapses, though individual relapses may result in severe residual disability. The course of MS varies, however, about 85-90% of individuals with MS demonstrate a relapsing pattern at onset, which transitions over time in the majority of untreated patients to a pattern of progressive worsening with few or no relapses or MRI activity.(11)
Secondary progressive multiple sclerosis (SPMS)	SPMS begins as RRMS, but over time the disease enters a stage of steady deterioration in function, unrelated to acute attacks. Most people with RRMS will transition to SPMS. In SPMS there is progressive worsening of symptoms over time with no definite periods of remission.(11)

<table>
<tr><td>Primary progressive multiple sclerosis (PPMS)</td><td>PPMS is characterized by worsening symptoms and disability from the start, rather than sudden attacks or relapses followed by recovery.(11) Currently ocrelizumab is the only DMA FDA approved for PPMS.(2,21)</td></tr>
<tr><td>2017 McDonald Criteria for the diagnosis of Multiple Sclerosis:</td><td>Diagnostic criteria for multiple sclerosis (MS) combining clinical, imaging, and laboratory evidence have evolved over time. The increasing incorporation of paraclinical assessments, especially imaging, to supplement clinical findings has allowed earlier, more sensitive, and more specific diagnosis.(9,10)

The diagnosis of MS requires elimination of more likely diagnoses and demonstration of dissemination of lesions in the CNS in space and time.(9)

Misdiagnosis of MS remains an issue in clinical practice, and several factors that potentially increase this risk have been identified. MS has heterogeneous clinical and imaging manifestations, which differ between patients over time. There is no single pathognomonic clinical feature or diagnostic test; diagnosis of MS relies on the integration of clinical, imaging, and laboratory findings. MRI abnormalities associated with other diseases and non-specific MRI findings, which are common in the general population, can be mistaken for MS. The increasingly strong focus on timely diagnosis to alleviate uncertainty for patients and allow initiation of disease-modifying therapies might also increase the risk of misdiagnosis.(9)

With increasing availability and use of MRI, incidental T2 hyperintensities on brain imaging are common, the subset of individuals with MRI findings that are strongly suggestive of MS lesions but with no neurological manifestations or other clear-cut explanation are said to have radiologically isolated syndrome. There is no consensus on whether patients with radiologically isolated syndrome will develop MS. Some practitioners argue that these patients have a high likelihood of developing MS while others argue that up to two-thirds of these patients will not receive a diagnosis of MS in 5 years. A consensus panel decided to require clinical manifestations to make the diagnosis of MS (2017 McDonald Criteria for the diagnosis of MS).(9)

The 2017 McDonald criteria to diagnose MS is shown in the chart below.(9,10)
<table>
<tr><th>Clinical Presentation</th><th>Additional Data needed to make MS diagnosis</th></tr>
<tr><td colspan="2">In a person with a typical attack/CIS at onset</td></tr>
<tr><td>Greater than or equal to 2 attacks and objective clinical evidence of greater than or equal to 2 lesions
OR
Greater than or equal to 2 attacks and objective clinical evidence of 1 lesion with historical evidence of prior attack involving lesion in different location</td><td>None. Dissemination in space* and dissemination in time** have been met</td></tr>
<tr><td>Greater than or equal to 2 attacks and objective clinical evidence of 1 lesion</td><td>ONE of these criteria:
Additional clinical attack implicating different CNS site
OR
Greater than or equal to 1 symptomatic or asymptomatic MS-typical T2 lesions in greater than or equal to 2 areas of CNS: periventricular, juxtacortical/cortical, infratentorial, or spinal cord</td></tr>
<tr><td>1 attack and objective clinical evidence of greater than or equal to 2 lesions</td><td>ONE of these criteria:
Additional clinical attack
OR
Simultaneous presence of both</td></tr>
</table>
</td></tr>
</table>

		enhancing and non-enhancing symptomatic or asymptomatic MS-typical MRI lesions OR New T2 or enhancing MRI lesion compared to baseline scan (without regard to timing of baseline scan) OR CSF specific (i.e., not in serum) oligoclonal bands
	1 attack and objective clinical evidence of 1 lesion	**ONE** of these criteria: Additional attack implicating different CNS site OR Greater than or equal to 1 MS-Typical symptomatic or asymptomatic T2 lesions in greater than or equal to 2 areas of CNS: periventricular, juxtacortical/cortical, infratentorial, or spinal cord **AND** **ONE** of these criteria: Additional clinical attack OR Simultaneous presence of both enhancing and non-enhancing symptomatic or asymptomatic MS-typical MRI lesions OR New T2 enhancing MRI lesion compared to baseline scan (without regard to timing of baseline scan) OR CSF-specific (i.e., not in serum) oligoclonal bands
	In a person with progression of disability from onset	
	Progression from onset	1 year of disability progression (retrospective or prospective) **AND** **TWO** of these criteria: Greater than or equal to 1 symptomatic or asymptomatic MS-typical T2 lesions (periventricular, juxtacortical/cortical, or infratentorial) **OR** Greater than or equal to 2 T2 spinal cord lesions **OR** CSF-specific (i.e., not in serum) oligoclonal bands

* - Dissemination in space is defined as one or more T2-hyperintense lesions that are characteristic of MS in 2 or more of four areas of the CNS (periventricular, cortical or juxtacortical, and infratentorial brain regions, and the spinal cord) demonstrated by an additional clinical attack implicating a different CNS site or by MRI.(9)

** - Dissemination in time is defined as simultaneous presence of gadolinium-enhancing and non-enhancing lesions at any time or by a new T2-hyperintense or gadolinium-enhancing lesion on follow-up MRI, with reference to a baseline scan, irrespective of the timing of the baseline MRI. The presence of CSF-specific oligoclonal bands does not demonstrate dissemination in time per se but can substitute for the requirement for demonstration of this measure.(9)

Treatment of MS	Both the Multiple Sclerosis Coalition and the American Academy of Neurology recommend initiating treatment with a DMA FDA approved for the patient's phenotype

	as soon as possible following the diagnosis of multiple sclerosis. There are several DMAs with at least 10 mechanisms of action available to people with MS. The factors affecting choice of therapy at any point in the disease course are complex and most appropriately analyzed and addressed through a shared decision-making process between the individual and the treating clinician.(4,7)
	
	The Multiple Sclerosis Coalition recommends that clinicians should consider prescribing a high efficacy medication such as alemtuzumab, cladribine, fingolimod, natalizumab or ocrelizumab for newly diagnosed individuals with highly active MS. Clinicians should also consider prescribing a high efficacy medication for individuals who have breakthrough activity on another DMA regardless of the number of previously used agents.(4) The American Academy of Neurology has recommended alemtuzumab, fingolimod, and natalizumab as options for patients with MS with highly active MS. There lacks a consensus for what constitutes as highly active MS, however.(7) The National Institute for Health and Care Excellence (NICE) defines rapidly evolving severe RRMS as two or more disabling relapses in 1 year, and one or more gadolinium-enhancing lesions on brain MRI or a significant increase in T2 lesion load compared with a previous MRI.(18)
	
	Lack of response to DMAs is hard to define, as most patients with MS are not free of all disease activity. Relapses or new MRI detected lesions may develop after initiation of a DMA and before the treatment becomes effective for patients. When determining efficacy, sufficient time for the DMA therapy to take full effect and patient adherence are important considerations. Evidence of one or more relapses, 2 or more unequivocally new MRI-detected lesions, or increased disability on examination while being treated with a DMA for a 1 year period suggests a sub-optimal response, an alternative regimen (e.g., different mechanism of action) should be considered to optimize therapeutic benefit.(6) A National MS Society consensus statement recommends changing from one disease modifying therapy to another only for medically appropriate reasons (e.g., lack of efficacy, adverse effects, or if better treatments options become available).(4)
	
	Existing MS therapies are partly effective in halting ongoing inflammatory tissue damage and clinical progression. MS pathogenesis is complex and probably heterogeneous among patient, suggesting that combination therapy strategies that target a range of disease mechanisms might be more effective than medications used as monotherapy. Although preliminary studies have provided favorable results, several subsequent large, randomized, controlled trials have had negative of conflicting results. There also may be more adverse reactions associated with combination therapies due to the additive effect.(13)
	
	In 2020 a Canadian MS working group published recommendations on optimal therapy in relapsing forms of MS. This group notes that there are few studies that have directly compared injectable and oral DMTs. A recent network meta-analysis suggested that pegylated interferon-β-1a and dimethyl fumarate have superior efficacy to other base therapies, there are insufficient data to demonstrate that one base injectable or oral DMT is superior to another. As a result, the choice of initial treatment will need to be individualized according to disease activity, severity, and comorbidities.(14)
	
	In addition to base therapies, the working group considers 5 DMTs to be of higher efficacy which although can be used as initial therapy, they are generally reserved for patients with a poor response or tolerability with a base therapy. Patients presenting with high disease activity or aggressive/rapidly evolving MS at onset could be considered to initiate therapy with one of these more effective therapies, but the most common treatment initiation is to start on a base therapy with the view of switching within 6 -12 months. The 5 agents considered to be of higher efficacy are:(14)
	
	• Oral agents
	  ○ Fingolimod
	  ○ Cladribine
	• Monoclonal antibodies

- Natalizumab
- Ocrelizumab
- Alemtuzumab

The MS working group discussed the criteria for switching therapies in RRMS and recommends a change in DMT is indicated for patients who meet any of the Major criteria below:(14)

	Minor	**Major**
Relapse rate	• One relapse in first 2 years of treatment	• Greater than or equal to 2 relapses in first year of treatment
Severity	• Mild • No functional impairment (school, work, daily activities, etc) • No motor/cerebellar/brain stem /sphincter involvement	• Moderate to severe • Functional impairment • Motor/cerebellar/brain stem/sphincter involvement
Recovery	• Full recovery at 6 months • No functional impairment • EDSS change from baseline less than or equal to 1 point at 6 months unless baseline EDSS greater than 5.5	• Incomplete recovery • Functional impairment • If EDSS at baseline was 0 then greater than a 1.5 point change from baseline • If EDSS greater than 0 but less than or equal to 5.5 at baseline then greater than 1 point change at 6 months • If EDSS greater than 5.5 any change would be a major concern
MRI	• One new lesion	• Greater than or equal to 3 new lesions during treatment excluding spinal cord lesions

		• Greater than 1 spinal cord lesion

The workgroup does note that on-treatment relapses should only be performed once the drug has achieved a full clinical effect (typically 2-6 months after drug initiation). Relapses that occur before the maximal efficacy of the drug has been reached should be given less weight, but major criteria should take precedence regardless of timing.(14)

For patients with SPMS the workgroup states that is generally advised to continue with the current DMT after onset of SPMS since many patients will have ongoing inflammatory disease and subclinical disease activity may worsen if treatment is withdrawn. A change in treatment may be warranted in patients with active SPMS who continue to have relapses or new MRI lesions, with the caveat that there is insufficient evidence to identify criteria for a suboptimal response in patients with SPMS.(14)

For patients with primary progressive MS clinicians should offer ocrelizumab to patients with active disease provided the benefits outweigh the risks. Caution is recommended when considering treatment for PPMS subgroups that are less likely to benefit from treatment, such as older patients, those with long-standing stable disease, and/or significant neurological deficits, since the limited benefits may not justify the risk associated with treatment. Rituximab may be considered as an alternative therapy for PPMS in regions that permit off-label use in MS due to cost or other considerations.(14)

The ICER evaluated a new IV treatment, ublituximab against current FDA and accepted use DMT for adults with RRMS. Only in the case of ublituximab vs placebo/no DMT is ublituximab superior rated. The ratings are noted below.(20)

Adults with RRMS

Treatment	Comparator	Evidence Rating
Ublitiximab	Natalizumab	I: Insufficient
	Ofatumumab	I: Insufficient
	Ocrelizumab	I: Insufficient
	Rituximab	I: Insufficient
	Fumarate class (dimethyl, diroximel, monomethyl)	C++: Comparable or better
	Fingolimod	C++: Comparable or better
	Ozanimod	C++: Comparable or better
	Ponesimod	C++: Comparable or better
	Siponimod	I: Insufficient
	Teriflunomide	B: Incremental
	Placebo/no DM	A: Superior

A: Superior - High certainty of a substantial (moderate-large) net health benefit
B: Incremental - High certainty of a small net health benefit
C++: Comparable or better - Moderate certainty of a comparable, small, or substantial net health benefit, with which certainty of at least a comparable net health benefit
I: Insufficient - Any situation where the level of certainty in the evidence is low

	ICER does note that payors should consider the following:(20) • Payors should remove barriers to access to rituximab for RMS patients who are appropriate candidates for this therapy. This includes coverage of biosimilar rituximab with little or no prior authorization given the lack of concern regarding use in appropriate patients and how inexpensive it is compared with other monoclonal antibodies of equal effectiveness • Payors should not unilaterally implement policies to switch RMS patients who are stable on their chosen DMT over to lower-cost biosimilar rituximab
Crohn's Disease (CD)	CD is an inflammatory condition that can affect any portion of the gastrointestinal tract from the mouth to the perianal area. Choice of therapy is dependent on the anatomic location of disease, the severity of disease, and whether the treatment goal is to induce remission or maintain remission.(12,16) The American Gastroenterological Association (AGA) 2021 guideline recommends the following:(12) • Biologic therapy: o The AGA suggest early introduction with a biologic, with or without an immunomodulator, rather than delaying their use until after failure of 5-aminosalicylates and/or corticosteroids o Anti-TNF (i.e., infliximab or adalimumab) and ustekinumab are recommended over no treatment for the induction and maintenance of remission o Vedolizumab is suggested over no treatment for the induction and maintenance of remission o AGA suggests against the use of natalizumab over no treatment for the induction and maintenance of remission o Patients naïve to biologic therapy, the AGA recommends infliximab, adalimumab, or ustekinumab over certolizumab pegol and suggests the use of vedolizumab over certolizumab pegol for the induction of remission o Patients with primary non-response to anti-TNF, the AGA recommends ustekinumab and suggests vedolizumab for induction of remission o Patients with secondary non-response to infliximab, the AGA recommends use of adalimumab or ustekinumab and suggests the use of vedolizumab for the induction of remission (if adalimumab was the first-line drug, there is indirect evidence to suggest using infliximab as a second-line agent) • DMARD therapy: o Corticosteroids are suggested over no treatment for the induction of remission, and are recommended against for maintenance of remission o Patients in corticosteroid induced remission or with quiescent moderate to severe CD, the AGA suggests thiopurines for maintenance of remission o Subcutaneous or intramuscular methotrexate are suggested over no treatment for the induction and maintenance of remission o The AGA recommends against the use of 5-aminosalicylates or sulfasalazine over no treatment for the induction or maintenance of remission o The AGA suggests against the use of thiopurines over no treatment for achieving remission and recommends biologic drug monotherapy over thiopurine monotherapy for induction of remission o The AGA suggests against the use of oral methotrexate monotherapy over no treatment for the induction and maintenance of remission • Combination therapy: o Patients that are naïve to biologics and immunomodulators, the AGA suggest use of infliximab in combination with thiopurines over infliximab monotherapy for the induction and maintenance of remission (combination infliximab with methotrexate may be more effective over infliximab monotherapy) o Patients that are naïve to biologics and immunomodulators, the AGA suggest use of adalimumab in combination with thiopurines over

	adalimumab monotherapy for the induction and maintenance of remission (combination adalimumab with methotrexate may be more effective over adalimumab monotherapy) o No recommendations are being made regarding the use of ustekinumab or vedolizumab in combination with thiopurines or methotrexate over biologic monotherapy for induction or maintenance or remission The 2018 American College of Gastroenterology (ACG) guideline recommends the following:(12) • Mild to moderately severe disease/low risk disease: o Sulfasalazine (in doses of 3-6 grams daily) is effective in colonic and/or ileocolonic CD, but not those with isolated small bowel disease o 5-aminosalicylic (ASA) suppositories and enema preparations are effective for induction and maintenance of remission in rectal and sigmoid disease o Conventional corticosteroids are primarily used for the treatment of flares, and are often used as a bridge until immunomodulators and/or biologic agents become effective o Controlled ileal release budesonide is effective for induction of remission in ileocecal disease • Moderate to severe disease/moderate to high risk disease o Corticosteroids are effective for short-term use in alleviating signs and symptoms of moderate to severely active CD, but do not induce mucosal healing and should be used sparingly o Azathioprine, 6-mercaptopurine, or MTX (15 mg once weekly) may be used in treatment of active disease and as adjunctive therapy for reducing immunogenicity against biologic therapy o TNF inhibitors should be used to treat CD that is resistant to treatment with corticosteroids and that is refractory to thiopurines or MTX o Natalizumab should be considered to be used for induction of symptomatic response and remission in patients with active Crohn's disease o Vedolizumab with or without an immunomodulator should be considered for induction of symptomatic remission for patients with moderate to severely active CD and objective evidence of active disease o Ustekinumab should be used in patients that have failed previous treatment with corticosteroids, thiopurines, MTX, or TNF inhibitors, or in patients with no prior TNF inhibitor exposure • Maintenance therapy: o Thiopurines or methotrexate should be considered once remission is induced with corticosteroids o TNF inhibitors, specifically infliximab, adalimumab, and certolizumab pegol, should be used in combination with azathioprine, MTX, or 6-mercaptopurine to maintain remission of TNF induced remission o Natalizumab should be used for maintenance of natalizumab-induced remission of Crohn's disease only if serum antibody to John Cunningham virus (JCV) is negative. Testing for anti-JCV antibody should be repeated every 6 months and treatment stopped if the result is positive o Vedolizumab should be used for maintenance of remission of vedolizumab induced remission o Ustekinumab should be used for maintenance of remission of ustekinumab induced remission
Safety	• **Briumvi** is contraindicated in:(19) o Active hepatitis B virus infection o History of life-threatening infusion reaction to Briumvi • **Lemtrada** has the following safety information:(1) o Boxed warning: Autoimmunity, infusion reactions, stroke, malignancies

	○ Contraindications: ▪ Known hypersensitivity or anaphylactic reactions to alemtuzumab or any of the excipients in Lemtrada ▪ Infection with human immunodeficiency virus (HIV) ▪ Active infection ○ Available only through a restricted distribution program • **Ocrevus** and **Ocrevus Zunovo** are contraindicated in:(2,21) ○ Active hepatitis B virus infection ○ History of life-threatening infusion reaction to ocrelizumab • **Tysabri** has the following safety information:(3) ○ Boxed warning: Progressive multifocal leukoencephalopathy (PML) ○ Contraindications: ▪ Patients who have or have had PML ▪ Patients who have had a hypersensitivity reaction to Tysabri ○ Available only through a restricted distribution program called the TOUCH Prescribing Program

REFERENCES

Number	Reference
1	Lemtrada prescribing information. Genzyme Corporation. May 2024.
2	Ocrevus prescribing information. Genentech, Inc. June 2024.
3	Tysabri prescribing information. Biogen, Inc. October 2023.
4	National Institute for Health and Care Excellence (NICE) Guideline. Multiple Sclerosis in Adults: Management (NG220). Published: 22 June 2022. Available at: https://www.nice.org.uk/guidance/ng220
5	Reference no longer used.
6	Rae-Grant A, Day GS, Marrie RA, et al. Practice Guideline Recommendations Summary: Disease-Modifying Therapies for Adults with Multiple Sclerosis. Neurology. 2018 Apr;90(17):777-788.
7	Corboy JR, Weinshenker BG, Wingerchuk DM. Comment on 2018 American Academy of Neurology Guidelines on Disease-Modifying Therapies in MS. Neurol. 2018 Apr;90(24):1106-1112.
8	Reference no longer used.
9	Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of Multiple Sclerosis: 2017 Revisions of the McDonald Criteria. Lancet Neurol. 2018 Feb;17(2):162-173.
10	National Multiple Sclerosis Society 2017 McDonald MS Diagnostic Criteria. Available at: https://www.nationalmssociety.org/for-professionals/for-healthcare-professionals/diagnosing-ms/diagnostic-criteria-workup
11	MS International Federation. Types of MS. Last updated: 12th March 2022. Available at: https://www.msif.org/about-ms/types-of-ms/
12	Feuerstein JD, Ho EY, Shmidt E, et al. American Gastroenterological Association (AGA) Clinical Practice Guidelines on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. Gastroenterol. 2021 Jun;160(7):2496-2508.
13	Conway D, Cohen JA. Combination Therapy in Multiple Sclerosis. Lancet Neurol. 2010 Mar;9(3):299-308.
14	Freedman MS, Devonshire V, Duquette P, et al. Treatment Optimization in Multiple Sclerosis: Canadian MS Working Group Recommendations. Can J Neurol Sci. 2020 Jul;47(4):437-455.
15	Reference no longer used.
16	Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol. 2018 Apr;113(4):481-517.
17	MS International Federation. Symptoms. Last updated: 25th October 2021. Available at: https://www.msif.org/about-ms/symptoms-of-ms/
18	National Institute for Health and Care Excellence (NICE). Ofatumumab for Treating Relapsing Multiple Sclerosis: Technology Appraisal Guidance (TA699). 2021 May. Available at: https://www.nice.org.uk/guidance/ta699

Number	Reference
19	Briumvi prescribing information. TG Therapeutics, Inc. December 2022.
20	McKenna A, Lin GA, Whittington MD, et al. Oral and Monoclonal Antibody Treatments for Relapsing Forms of Multiple Sclerosis: Effectiveness and Value. A Summary from the Institute for Clinical and Economic Review's (ICER) New England Comparative Effectiveness Public Advisory Council. J Manag Care Spec Pharm. 2023 Jul;29(7):10.18553.
21	Ocrevus Zunovo prescribing information. Genentech, Inc. September 2024.

POLICY AGENT SUMMARY – MEDICAL PRIOR AUTHORIZATION

HCPC Codes	Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
J2329	Briumvi	ublituximab-xiiy soln for iv infusion	150 MG/6ML	M ; N ; O ; Y	N		
J0202	Lemtrada	alemtuzumab iv inj	12 MG/1.2ML	M ; N ; O ; Y	N		
J2350	Ocrevus	ocrelizumab soln for iv infusion	300 MG/10ML	M ; N ; O ; Y	N		
J2351	Ocrevus zunovo	ocrelizumab-hyaluronidase-ocsq inj	920-23000 MG-UT/23ML	M ; N ; O ; Y	N		
J2323	Tysabri	natalizumab for iv inj conc	300 MG/15ML	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Ocrevus zunovo	ocrelizumab-hyaluronidase-ocsq inj	920-23000 MG-UT/23ML	1	Vial	180	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Briumvi	ublituximab-xiiy soln for iv infusion	150 MG/6ML	Commercial ; HIM ; ResultsRx
Lemtrada	alemtuzumab iv inj	12 MG/1.2ML	Commercial ; HIM ; ResultsRx
Ocrevus	ocrelizumab soln for iv infusion	300 MG/10ML	Commercial ; HIM ; ResultsRx
Ocrevus zunovo	ocrelizumab-hyaluronidase-ocsq inj	920-23000 MG-UT/23ML	Commercial ; HIM ; ResultsRx
Tysabri	natalizumab for iv inj conc	300 MG/15ML	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Ocrevus zunovo	ocrelizumab-hyaluronidase-ocsq inj	920-23000 MG-UT/23ML	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Briumvi	**Initial Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. The requested agent is eligible for continuation of therapy AND ONE of the following: **Agents Eligible for Continuation of Therapy** **Briumvi** (ublituximab-xiiy) 1. The patient has been treated with the requested agent within the past 210 days **OR** 2. The prescriber states the patient has been treated with the requested agent within the past 210 days AND is at risk if therapy is changed **OR** B. BOTH of the following: 1. ONE of the following: A. The patient has a diagnosis of a relapsing form of multiple sclerosis (MS) **OR** B. The patient has another FDA labeled indication for the requested agent and route of administration **AND** 2. If the patient has an FDA labeled indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support for using the requested agent for the patient's age for the requested indication **AND** 2. If starting therapy, the patient has been tested for hepatitis B virus and determined to not have active hepatitis B viral infection **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (i.e., neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient will NOT be using the requested agent in combination with another disease modifying agent (DMA) for the requested indication (Please refer to "MS Disease Modifying Agents" list in the "Contraindicated as Concomitant Therapy" table) **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 6. The requested quantity (dose) is within FDA labeled dosing for the requested indication **Length of Approval:** 12 months NOTE: For patients initiating therapy, approval will include 4 vials for induction dosing (one 150 mg first infusion dose [1 vial] and one 450 mg second infusion dose [3 vials]) and two 450 mg maintenance doses (6 vials) **Renewal Evaluation** **Target Agent(s)** will be approved when ALL the following are met: 1. The patient has been previously approved for the requested agent through the plan's Medical Drug Review process [Note: patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. The patient has had clinical benefit from treatment with the requested agent **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (i.e., neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient will NOT be using the requested agent in combination with another disease modifying agent (DMA) for the requested indication (Please refer to "MS Disease Modifying Agents" list in the "Contraindicated as Concomitant Therapy" table) **AND**

Module	Clinical Criteria for Approval
	5. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 6. The requested quantity (dose) is within FDA labeled dosing for the requested indication **Length of Approval:** 12 months
Lemtrada	

Preferred Agent(s)	Non-Preferred Agent(s)
Avonex (interferon β-1a) **Betaseron** (interferon β-1b) dimethyl fumarate fingolimod glatiramer **Glatopa** (glatiramer) **Kesimpta** (ofatumumab) **Mavenclad** (cladribine) **Mayzent** (siponimod) **Plegridy** (peginterferon β-1a) **Rebif** (interferon β-1a) teriflunomide **Vumerity** (diroximel fumarate) **Zeposia** (ozanimod)**	**Aubagio** (teriflunomide)* **Bafiertam** (monomethyl fumarate) **Copaxone** (glatiramer)* **Extavia** (interferon β-1b) **Gilenya** (fingolimod)* **Ponvory** (ponesimod) **Tascenso ODT** (fingolimod) **Tecfidera** (dimethyl fumarate)*

*generic available
**target in a different program

Initial Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. ONE of the following:
   A. The requested agent is eligible for continuation of therapy AND ONE of the following:

Agents Eligible for Continuation of Therapy
Lemtrada (alemtuzumab)

      1. The patient has been treated with the requested agent within the past 90 days **OR**
      2. The prescriber states that the patient has been treated with the requested agent within the past 90 days AND is at risk if therapy is changed **OR**
   B. BOTH of the following:
      1. ONE of the following:
         A. BOTH of the following:
            1. The patient has a diagnosis of ONE of the following relapsing forms of multiple sclerosis (MS):
               A. Relapsing-remitting disease (RRMS) **OR**
               B. Active secondary progressive disease (SPMS) **AND**
            2. ONE of the following:
               A. The patient has highly active MS disease activity AND BOTH of the following:
                  1. The patient has greater than or equal to 2 relapses in the previous year **AND**
                  2. ONE of the following:
                     A. The patient has greater than or equal to 1 gadolinium enhancing lesion on MRI **OR**

Module	Clinical Criteria for Approval

B. The patient has a significant increase in T2 lesion load compared with a previous MRI **OR**

B. The patient has been treated with at least 3 MS agents from different drug classes (see MS disease modifying agents drug class table) **OR**

C. ONE of the following:

1. The patient has tried and had an inadequate response to TWO preferred agents FDA labeled for the treatment of the requested indication **OR**
2. The patient has an intolerance or hypersensitivity to TWO preferred agents FDA labeled for the treatment of the requested indication **OR**
3. The patient has an FDA labeled contraindication to ALL preferred agents FDA labeled for the treatment of the requested indication **OR**
4. There is support for using the requested agent over ALL preferred agents FDA labeled for the treatment of the requested indication **OR**

B. The patient has another FDA labeled indication for the requested agent and route of administration **AND**

2. If the patient has an FDA labeled indication, then ONE of the following:
   A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR**
   B. There is support for using the requested agent for the patient's age for the requested indication **AND**
2. The patient will be receiving anti-viral prophylaxis for herpetic viral infections **AND**
3. The prescriber is a specialist in the area of the patient's diagnosis (i.e., neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND**
4. The patient will NOT be using the requested agent in combination with another disease modifying agent (DMA) for the requested indication (Please refer to "MS Disease Modifying Agents" list in the "Contraindicated as Concomitant Therapy" table) **AND**
5. The patient does NOT have any FDA labeled contraindications to the requested agent **AND**
6. ONE of the following:
   A. The patient has NOT received treatment with the requested agent **OR**
   B. The patient has received treatment with the requested agent AND BOTH of the following:
      1. The prescriber has provided the number of doses and treatment courses the patient has received **AND**
      2. The patient has NOT received 2 or more treatment courses with the requested agent **AND**
7. The requested quantity (dose) is within FDA labeled dosing for the requested indication

Length of Approval: 12 months; for the diagnosis of RRMS or SPMS approve for remainder of annual dose, up to 5 doses for first treatment course and up to 3 doses for second treatment course

FDA Labeled Indication	FDA Approved Agents
Clinically Isolated Syndrome (CIS)	Aubagio, Avonex, Bafiertam, Betaseron, Copaxone, Extavia, Gilenya, Glatopa, Kesimpta, Mayzent, Plegridy, Ponvory, Rebif, Tascenso ODT, Tecfidera, Vumerity, Zeposia
Relapsing Remitting Multiple Sclerosis (RRMS)	Aubagio, Avonex, Bafiertam, Betaseron, Copaxone, Extavia, Gilenya, Glatopa, Kesimpta, Mavenclad, Mayzent,

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	Plegridy, Ponvory, Rebif, Tascenso ODT, Tecfidera, Vumerity, Zeposia
Active Secondary Progressive Multiple Sclerosis (SPMS)	Aubagio, Avonex, Bafiertam, Betaseron, Copaxone, Extavia, Gilenya, Glatopa, Kesimpta, Mavenclad, Mayzent, Plegridy, Ponvory, Rebif, Tascenso ODT, Tecfidera, Vumerity, Zeposia

Renewal Evaluation

Target Agent(s) will be approved when ALL the following are met:

1. The patient has been previously approved for the requested agent through the plan's Medical Drug Review process [Note: patients not previously approved for the requested agent will require initial evaluation review] **AND**
2. The patient has had clinical benefit from treatment with the requested agent **AND**
3. ALL of the following:
   A. The patient will be receiving anti-viral prophylaxis for herpetic viral infections **AND**
   B. The prescriber has provided the number of doses and treatment courses the patient has received **AND**
   C. The patient has NOT received 2 or more treatment courses with the requested agent **AND**
4. The prescriber is a specialist in the area of the patient's diagnosis (i.e., neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND**
5. The patient will NOT be using the requested agent in combination with another disease modifying agent (DMA) for the requested indication (Please refer to "MS Disease Modifying Agents" list in the "Contraindicated as Concomitant Therapy" table) **AND**
6. The patient does NOT have any FDA labeled contraindications to the requested agent **AND**
7. The requested quantity (dose) is within FDA labeled dosing for the requested indication

Length of Approval: 12 months; for the diagnosis of RRMS or SPMS approve for remainder of annual dose, up to 5 doses for first treatment course and up to 3 doses for second treatment course

Ocrevus, Ocrevus Zunovo

Initial Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. ONE of the following:
   A. The requested agent is eligible for continuation of therapy AND ONE of the following:

Agents Eligible for Continuation of Therapy
Ocrevus (ocrelizumab), **Ocrevus Zunovo** (ocrelizumab-hyaluronidase)

      1. The patient has been treated with the requested agent within the past 210 days **OR**
      2. The prescriber states the patient has been treated with the requested agent within the past 210 days AND is at risk if therapy is changed **OR**
   B. BOTH of the following:
      1. ONE of the following:
         A. The patient has a diagnosis of a relapsing form of multiple sclerosis (MS) **OR**
         B. The patient has a diagnosis of primary progressive multiple sclerosis (PPMS) **OR**

Module	Clinical Criteria for Approval
	C. The patient has another FDA labeled indication for the requested agent and route of administration **AND** 2. If the patient has an FDA labeled indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support of using the requested agent for the patient's age for the requested indication **AND** 2. If starting therapy, the patient has been tested for hepatitis B virus and determined to not have active hepatitis B viral infection **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (i.e., neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient will NOT be using the requested agent in combination with another disease modifying agent (DMA) for the requested indication (Please refer to "MS Disease Modifying Agents" list in the "Contraindicated as Concomitant Therapy" table) **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 6. ONE of the following: A. The requested agent is Ocrevus Zunovo and ONE of the following: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. BOTH of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) is within FDA labeled dosing for the requested indication **OR** B. The requested agent is not Ocrevus Zunovo and the requested quantity (dose) is within FDA labeled dosing for the requested indication **Length of Approval:** 12 months. NOTE: For patients initiating therapy with Ocrevus, approval will include two initial 300 mg loading doses (2 vials) and two 600 mg maintenance doses (4 vials). For Ocrevus Zunovo, dosage is 1 vial every 6 months. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL the following are met: 1. The patient has been previously approved for the requested agent through the plan's Medical Drug Review process [Note: patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. The patient has had clinical benefit from treatment with the requested agent **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (i.e., neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient will NOT be using the requested agent in combination with another disease modifying agent (DMA) for the requested indication (Please refer to "MS Disease Modifying Agents" list in the "Contraindicated as Concomitant Therapy" table) **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 6. ONE of the following: A. The requested agent is Ocrevus Zunovo and ONE of the following: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. BOTH of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) is within FDA labeling for the requested indication **OR** B. The requested agent is not Ocrevus Zunovo and the requested quantity (dose) is within FDA labeled dosing for the requested indication

Module	Clinical Criteria for Approval
	Length of Approval: 12 months
Tysabri	**Preferred Biologic Agents for Crohn's Disease**

Step 1a	Step 1b (Directed to ONE TNF inhibitor) NOTE: Please see Step 1a for preferred TNF inhibitors	Step 2 (Directed to ONE Step 1 agent)	Step 3a (Directed to TWO Step 1 agents)	Step 3b (Directed to TWO agents from Step 1 and/or Step 2)	Step 3c (directed to THREE Step 1 agents)
SC: adalimumab product(s)**, Entyvio, Skyrizi, Tremfya, ustekinumab product(s)^^	Oral: Rinvoq	SC: Omvoh	SC: Cimzia, Zymfentra	N/A	N/A

** Allowable preferred adalimumab product(s): Adalimumab-aaty, Adalimumab-adaz, Hadlima, Simlandi
^^ Allowable preferred ustekinumab product(s): Selarsdi, Steqeyma, Yesintek

Initial Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. ONE of the following:
   A. The requested agent is eligible for continuation of therapy AND ONE of the following:

Agents Eligible for Continuation of Therapy
Tysabri (natalizumab)

      1. The patient has been treated with the requested agent within the past 90 days **OR**
      2. The prescriber states the patient has been treated with the requested agent within the past 90 days AND is at risk if therapy is changed **OR**
   B. BOTH of the following:
      1. ONE of the following:
         A. The patient has a diagnosis of moderately to severely active Crohn's disease (CD) AND ALL of the following:
            1. The requested agent, including route of administration, is FDA labeled for CD **AND**
            2. The requested agent will NOT be used in combination with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) **AND**
            3. ONE of the following:
               A. The patient has tried and had an inadequate response to ONE conventional agent (i.e., 6-mercaptopurine, azathioprine, corticosteroids [e.g., prednisone, budesonide EC capsule], methotrexate) used in the treatment of CD for at least 3 months **OR**

Module	Clinical Criteria for Approval
	B. The patient has an intolerance or hypersensitivity to ONE of the conventional agents used in the treatment of CD **OR** C. The patient has an FDA labeled contraindication to ALL of the conventional agents used in the treatment of CD **OR** D. The patient's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in compendia for the treatment of CD **AND** 4. If the client has preferred biologic agents for the treatment of CD, then ONE of the following: A. The patient has tried and had an inadequate response to at least ONE preferred biologic agent for the treatment of CD used for at least 3 months **OR** B. The patient has an intolerance or hypersensitivity to ONE preferred biologic agent for the treatment of CD **OR** C. The patient has an FDA labeled contraindication to ALL preferred biologic agents for the treatment of CD **AND** 5. The patient will NOT be using the requested agent in combination with an immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors) for the requested indication (Please refer to "Immunomodulatory Agents NOT to be used Concomitantly" list in the "Contraindicated as Concomitant Therapy" table) **OR** B. BOTH of the following: 1. The patient has a diagnosis of a relapsing form of multiple sclerosis (MS) **AND** 2. The patient will NOT be using the requested agent in combination with another disease modifying agent for the requested indication (Please refer to "MS Disease Modifying Agents" list in the "Contraindicated as Concomitant Therapy" table **OR** C. The patient has another FDA labeled indication for the requested agent and route of administration **AND** 2. If the patient has an FDA labeled indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support for using the requested agent for the patient's age for the requested indication **AND** 2. The prescriber is a specialist in the area of the patient's diagnosis (e.g., gastroenterologist for the diagnosis of Crohn's disease, neurologist for the diagnosis of MS) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 3. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 4. The requested quantity (dose) is within FDA labeled dosing for the requested indication **Length of Approval:** 16 weeks for Crohn's disease;12 months for all other FDA labeled indications **Compendia Allowed:** AHFS, or DrugDex 1 or 2a level of evidence **Renewal Evaluation**

Module	Clinical Criteria for Approval
	Target Agent(s) will be approved when ALL the following are met: 1. The patient has been previously approved for the requested agent through the plan's Medical Drug Review process [Note: patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. The patient has had clinical benefit from treatment with the requested agent **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., gastroenterologist for the diagnosis of Crohn's disease, neurologist for the diagnosis of MS) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. If the patient has a diagnosis of multiple sclerosis (MS), the patient will NOT be using the requested agent in combination with another disease modifying agent (DMA) for the requested indication (Please refer to "MS Disease Modifying Agents" list in the "Contraindicated as Concomitant Therapy" table) **AND** 5. If the patient has a diagnosis of Crohn's disease (CD), the patient will NOT be using the requested agent in combination with an immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors) for the requested indication (Please refer to "Immunomodulatory Agents NOT to be used Concomitantly" list in the "Contraindicated as Concomitant Therapy" table) **AND** 6. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 7. The requested quantity (dose) is within FDA labeled dosing for the requested indication **Length of Approval:** 12 months

CLASS AGENTS

Class	Class Drug Agents
CD20 monoclonal antibody	
CD20 monoclonal antibody	BRIUMVI*ublituximab-xiiy soln for iv infusion
CD20 monoclonal antibody	KESIMPTA*Ofatumumab Soln Auto-Injector
CD20 monoclonal antibody	OCREVUS*Ocrelizumab Soln For IV Infusion
CD20 Monoclonal antibody	
CD20 Monoclonal antibody	OCREVUS*ZUNOVO*ocrelizumab-hyaluronidase-ocsq inj
CD52 monoclonal antibody	
CD52 monoclonal antibody	LEMTRADA*Alemtuzumab IV Inj
Fumarates	
Fumarates	BAFIERTAM*Monomethyl Fumarate Capsule Delayed Release
Fumarates	TECFIDERA*Dimethyl Fumarate Capsule Delayed Release
Fumarates	VUMERITY*Diroximel Fumarate Capsule Delayed Release
Glatiramer	
Glatiramer	COPAXONE*Glatiramer Acetate Soln Prefilled Syringe
Glatiramer	GLATOPA*Glatiramer Acetate Soln Prefilled Syringe
IgG4k monoclonal antibody	
IgG4k monoclonal antibody	TYSABRI*Natalizumab for IV Inj Conc
Interferons	
Interferons	AVONEX*Interferon beta-1a injection
Interferons	BETASERON*Interferon beta-1b injection
Interferons	EXTAVIA*Interferon beta-1b injection
Interferons	PLEGRIDY*Peginterferon beta-1a injection
Interferons	REBIF*Interferon beta-1a injection
Purine antimetabolite	
Purine antimetabolite	MAVENCLAD*Cladribine Tab Therapy Pack
Pyrimidine synthesis inhibitor	

Class	Class Drug Agents
Pyrimidine synthesis inhibitor	AUBAGIO*Teriflunomide Tab
Sphingosine 1-phosphate (SIP) receptor modulator	
Sphingosine 1-phosphate (SIP) receptor modulator	GILENYA*Fingolimod HCl Cap
Sphingosine 1-phosphate (SIP) receptor modulator	MAYZENT*Siponimod Fumarate Tab
Sphingosine 1-phosphate (SIP) receptor modulator	PONVORY*Ponesimod Tab
Sphingosine 1-phosphate (SIP) receptor modulator	TASCENSO*fingolimod lauryl sulfate tablet disintegrating
Sphingosine 1-phosphate (SIP) receptor modulator	ZEPOSIA*Ozanimod capsule

CONTRAINDICATION AGENTS

Contraindicated as Concomitant Therapy
MS Disease Modifying Agents (DMAs) Aubagio (teriflunomide) Avonex (interferon b-1a) Bafiertam (monomethyl fumarate) Betaseron (interferon b-1b) Briumvi (ublituximab-xiiy) Copaxone (glatiramer) dimethyl fumarate Extavia (interferon b-1b) fingolimod Gilenya (fingolimod) glatiramer Glatopa (glatiramer) Kesimpta (ofatumumab) Lemtrada (alemtuzumab) Mavenclad (cladribine) Mayzent (siponimod) Ocrevus (ocrelizumab) Ocrevus Zunovo (ocrelizumab-hyaluronidase) Plegridy (peginterferon b-1a)

Contraindicated as Concomitant Therapy
Ponvory (ponesimod) Rebif (interferon b-1a) Tascenso ODT (fingolimod) Tecfidera (dimethyl fumarate) teriflunomide Tysabri (natalizumab) Vumerity (diroximel fumarate) Zeposia (ozanimod) **Immunomodulatory Agents NOT to be used Concomitantly** Abrilada (adalimumab-afzb) Actemra (tocilizumab) Adalimumab Adbry (tralokinumab-ldrm) Amjevita (adalimumab-atto) Arcalyst (rilonacept) Avsola (infliximab-axxq) Avtozma (tocilizumab-anoh) Benlysta (belimumab) Bimzelx (bimekizumab-bkzx) Cibinqo (abrocitinib) Cimzia (certolizumab) Cinqair (reslizumab) Cosentyx (secukinumab) Cyltezo (adalimumab-adbm) Dupixent (dupilumab) Ebglyss (lebrikizumab-lbkz)

Contraindicated as Concomitant Therapy
Enbrel (etanercept)
Entyvio (vedolizumab)
Fasenra (benralizumab)
Hadlima (adalimumab-bwwd)
Hulio (adalimumab-fkjp)
Humira (adalimumab)
Hyrimoz (adalimumab-adaz)
Idacio (adalimumab-aacf)
Ilaris (canakinumab)
Ilumya (tildrakizumab-asmn)
Imuldosa (ustekinumab-srlf)
Inflectra (infliximab-dyyb)
Infliximab
Kevzara (sarilumab)
Kineret (anakinra)
Leqselvi (deuruxolitinib)
Litfulo (ritlecitinib)
Nemluvio (nemolizumab-ilto)
Nucala (mepolizumab)
Olumiant (baricitinib)
Omlyclo (omalizumab-igec)
Omvoh (mirikizumab-mrkz)
Opzelura (ruxolitinib)
Orencia (abatacept)
Otezla (apremilast)
Otulfi (ustekinumab-aauz)
Pyzchiva (ustekinumab-ttwe)

Contraindicated as Concomitant Therapy
Remicade (infliximab)
Renflexis (infliximab-abda)
Riabni (rituximab-arrx)
Rinvoq (upadacitinib)
Rituxan (rituximab)
Rituxan Hycela (rituximab/hyaluronidase human)
Ruxience (rituximab-pvvr)
Saphnelo (anifrolumab-fnia)
Selarsdi (ustekinumab-aekn)
Siliq (brodalumab)
Simlandi (adalimumab-ryvk)
Simponi (golimumab)
Simponi ARIA (golimumab)
Skyrizi (risankizumab-rzaa)
Sotyktu (deucravacitinib)
Spevigo (spesolimab-sbzo) subcutaneous injection
Stelara (ustekinumab)
Steqeyma (ustekinumab-stba)
Taltz (ixekizumab)
Tezspire (tezepelumab-ekko)
Tofidence (tocilizumab-bavi)
Tremfya (guselkumab)
Truxima (rituximab-abbs)
Tyenne (tocilizumab-aazg)
Tysabri (natalizumab)
Ustekinumab
Velsipity (etrasimod)

Contraindicated as Concomitant Therapy
Wezlana (ustekinumab-auub)
Xeljanz (tofacitinib)
Xeljanz XR (tofacitinib extended release)
Xolair (omalizumab)
Yesintek (ustekinumab-kfce)
Yuflyma (adalimumab-aaty)
Yusimry (adalimumab-aqvh)
Zeposia (ozanimod)
Zymfentra (infliximab-dyyb)