Generic Name: N/A

Therapeutic Class or Brand Name: Multiple Sclerosis Agents

Applicable Drugs (if Therapeutic Class): Avonex® (interferon beta-1a), Aubagio® (teriflunomide), Bafiertam™ (monomethyl fumarate), Betaseron®(interferon beta-1b), Briumvi®(Ublituximab), Copaxone® (glatiramer), Extavia® (interferon beta-1b), Gilenya® (fingolimod), Glatopa™(glatiramer), Kesimpta® (ofatumumab), Lemtrada® (alemtuzumab), Mavenclad® (cladribine), Mayzent® (siponimod), Ocrevus™ (ocrelizumab), Plegridy®(peginterferon beta-1a), Ponvory® (ponesimod), Rebif® (interferonbeta-1a), Tecfidera® (dimethyl fumarate), Tysabri® (natalizumab), Vumerity™ (diroximel fumarate), Zeposia® (ozanimod)

Preferred: Avonex® (interferon beta-1a), Betaseron® (interferon beta-1b), dimethyl fumarate (generic), fingolimod (generic), glatiramir (generic), Kesimpta® (ofatumumab), Mayzent® (siponimod), Plegridy® (peginterferon beta-1a), Vumerity™ (diroximel fumarate), Zeposia® (ozanimod)

Non-preferred: Aubagio® (teriflunomide), Bafiertam™ (monomethyl fumarate), Briumvi®(Ublituximab), Copaxone®(glatiramer), Extavia® (interferon beta-1b), Gilenya® (fingolimod), Glatopa™ (glatiramer), Lemtrada® (alemtuzumab), Mavenclad® (cladribine), Ocrevus™(ocrelizumab), Ponvory® (ponesimod), Rebif® (interferon beta-1a), Tecfidera® (dimethyl Fumarate), Tysabri® (natalizumab)

Date of Origin: 5/26/2020

Date Last Reviewed / Revised: 1/1/2023

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criteria I-VI are met)

I. Documented diagnosis of multiple sclerosis AND the requested medication is used for an FDA-approved indication, or use is supported by current clinical practice guidelines. Refer to Table 1 for medication specific criteria.

II. The patient meets specific criteria listed for the requested medication in Table 1.

III. If request is for a non-preferred agent, must have a documented trial and failure of, intolerance, or contraindication to two preferred products (refer to plan document for the list of preferred products).

IV. Treatment must be prescribed by or in consultation with a neurologist or a multiple sclerosis physician specialist.

V. The patient has no known contraindication to the requested agent.

VI. Refer to the plan document for the list of preferred products. If the request is for a brand medication for which a generic is available, there must be a documented treatment failure or contraindication to the generic medication.

EXCLUSION CRITERIA

- Coadministration of any multiple sclerosis agent with any other disease-modifying therapy for the treatment of multiple sclerosis therapy.
- For Gilenya, Mayzent, Ponvory and Zeposia, the patient has no myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization, or Class III or IV heart failure in the last 6 months.
- Medication specific treatment exclusion as noted in Table 1.

OTHER CRITERIA

- Table 1

Agents	Medication Specific Criteria	Dosing Limits
Injectable and Infusions Agents		
Avonex® (interferon beta-1a)	○ CIS, RRMS, SPMS ○ ≥ 18 years	30 mcg IM once per week (4 injections per 28 days)
Betaseron®, Extavia® (interferon beta-1b)	○ CIS, RRMS, SPMS ○ ≥ 18 years	0.25 mg SC every other day (14 injections per 28 days)
Briumvi®(Ublituximab)	○ CIS, RRMS, SPMS ○ ≥ 18 years ○ Must be screened for Hep B and does not have an active Hepatitis B infection ○ All necessary immunizations administered 6 weeks prior to treatment initiation	150mg on day 1, followed by 450mg two weeks later, subsequent dose of 450mg administered once every 24 weeks thereafter
Copaxone®, Glatopa® (glatiramer)	○ CIS, RRMS, SPMS ○ ≥ 18 years	20 mg SC once daily (30 injections per 30 days) or 40 mg SC 3 times per week (12 injections per 28 days)
Kesimpta® (ofatumumab)	○ CIS, RRMS, SPMS ○ ≥ 18 years ○ Must be screened for Hepatitis B and does not have an active Hepatitis B infection ○ Serum immunoglobulin screening completed	Loading: 20 mg administered at Week 0, 1, and 2 Maintenance: 20 mg SC monthly starting at week 4

	○ Must not be pregnant or plan to become pregnant	
Lemtrada® (alemtuzumab)	○ RRMS, SPMS ○ ≥ 18 years ○ Must not be infected with HIV ○ CBC and serum creatinine levels ○ History of varicella OR has had the varicella-zoster vaccination OR has evidence of immunity (positive antibodies) ○ All necessary immunizations administered 6 weeks prior to treatment initiation	12 mg/day IV on 5 consecutive days (total 60 mg) then 12 mg IV daily for 3 consecutive days (total 36 mg)12 months later
Ocrevus™ (ocrelizumab)	○ PPMS, CIS, RRMS, SPMS ○ ≥ 18 years ○ Must be screened for Hep B and does not have an active Hepatitis B infection ○ All necessary immunizations administered 6 weeks prior to treatment initiation	300 mg IV on day 1, followed by 300 mg IV 2 weeks later, subsequent doses of 600 mg IV are administered once every 6 months (beginning 6 months after the first 300 mg dose)
Plegridy® (peginterferon beta-1a)	○ CIS, RRMS, SPMS ○ ≥ 18 years	Loading: 63 mcg SC on day 1, 94 mcg SC on day 15, then 125 mcg SC on day 29 Maintenance: 2 injections per 28 days.
Rebif® (interferon beta-1a)	○ CIS, RRMS, SPMS ○ ≥ 18 years	44 mcg SC 3 times per week (12 injections per 28 days)
Tysabri® (natalizumab)	○ CIS, RRMS, SPMS ○ ≥ 18 years ○ Must be evaluated for anti-JCV (John Cunningham virus) antibody test (ELISA [enzyme-linked immunosorbent assay])	300 mg IV infusion every 4 weeks
Oral Agents		
Aubagio® (neriflunomide)	○ CIS, RRMS, SPMS ○ ≥ 18 years ○ Must not be pregnant	7 or 14 mg orally once daily (30 tablets per 30 days)

	○ Must be screened for TB and does not have an active or latent TB ○ Will not be used with leflunomide ○ Must not have hepatic impairment (baseline LFT, bilirubin levels), and CBC completed	
Bafiertam™ (monomethyl fumarate)	○ CIS, RRMS, SPMS ○ ≥ 18 years ○ Must not have hepatic impairment (baseline LFT, bilirubin levels) ○ Lymphocyte count, and CBC completed	190 mg twice a day (120 capsules of 95 mg capsule per 30 days)
Gilenya® (fingolimod)	○ CIS, RRMS, SPMS ○ ≥ 10 years ○ Baseline LFT, bilirubin levels, and CBC must be completed ○ Must be screened for TB and does not have an active or latent TB ○ Baseline EKG is completed ○ Baseline ophthalmic examination is completed ○ Evidence of varicella-zoster vaccination, history of chickenpox, or evidence of immunity ○ There is no acute or chronic infection ○ Must not be pregnant or plan to become pregnant	30 capsules per 30 days Adults: 0.5 mg orally once daily Pediatric: ≥10 years of age and ≤40 kg: 0.25 mg orally once daily ≥10 years of age and >40 kg: 0.5 mg orally once daily
Mavenclad® (cladribine)	○ RRMS, SPMS ○ ≥ 18 years ○ Patient does not have a current malignancy ○ Patient does not have clinically isolated syndrome ○ Must not be pregnant or plan to become pregnant ○ All necessary immunizations administered 4-6 weeks prior to treatment initiation	3.5 mg/kg orally over a 2-year treatment course, administered as 1.75 mg/kg in each year, no more than 20 mg per day

Mayzent® (siponimod)	○ CIS, RRMS, SPMS ○ ≥ 18 years ○ Baseline LFT, bilirubin levels, and CBC must be completed ○ Must be screened for TB and does not have an active or latent TB ○ Baseline ECG is completed ○ Baseline ophthalmic examination is completed ○ Evidence of varicella-zoster vaccination, history of chickenpox, or evidence of immunity ○ There is no acute or chronic infection ○ Must not be pregnant or plan to become pregnant	CYP2C9 Genotype *1/*1, *1/*2, or *2/*2: 0.25 mg orally once daily on Days 1 and 2, then 0.5 mg once daily on Day 3, then 0.75 mg once daily on Day 4, then 1.25 mg once daily on Day 5, then 2 mg once daily, beginning on Day 6 CYP2C9 Genotype *1/*3 or *2/*3: 0.25 mg orally once daily on Days 1 and 2, then 0.5 mg once daily on Day 3, then 0.75 mg once daily on Day 4, then 1 mg once daily, beginning on Day 5
Ponvory® (ponesimod)	○ CIS, RRMS, SPMS ○ ≥ 18 years ○ Baseline LFT, bilirubin levels, and CBC must be completed ○ Must be screened for TB and does not have an active or latent TB ○ Baseline ECG is completed ○ Baseline ophthalmic examination is completed ○ Evidence of varicella-zoster vaccination, history of chickenpox, or evidence of immunity ○ There is no acute or chronic infection ○ Must not be pregnant or plan to become pregnant	Initial Dosage: One Ponvory® Starter Pack (14 tablets per 14 days) Maintenance: 20 mg once daily (30 tablets per 30 days)
Tecfidera® (dimethyl fumarate)	○ CIS, RRMS, SPMS ○ ≥ 18 years	240 mg orally twice daily (60 capsules per 30 days)
Vumerity™ (diroximel fumarate)	○ CIS, RRMS, SPMS ○ ≥ 18 years ○ Baseline LFT, bilirubin levels, and CBC must be completed	462 mg orally twice daily (120 capsules per 30 days)

	○ Treatment failure or contraindication to generic Tecfidera (dimethyl fumarate)	
Zeposia® (ozanimod)	○ CIS, RRMS, SPMS ○ ≥ 18 years ○ Baseline LFT, bilirubin levels, and CBC must be completed ○ Must be screened for TB and does not have an active or latent TB ○ Baseline ECG is completed ○ Baseline ophthalmic examination is completed ○ Evidence of varicella-zoster vaccination, history of chickenpox, or evidence of immunity ○ There is no acute or chronic infection ○ Must not be pregnant or plan to become pregnant ○ Patient has no history of severe sleep apnea	0.92 mg once daily (30 capsules per 30 days)
IV: intravenously. SC: subcutaneously. IM: intramuscularly. LFT: liver function test. CBC: complete blood count. ECG: electrocardiogram. TB: tuberculosis. CIS: clinically isolated syndrome. PPMS: primary progressive multiple sclerosis. RRMS: relapsing-remitting multiple sclerosis. SPMS: secondary progressive multiple sclerosis.		

QUANTITY / DAYS SUPPLY RESTRICTIONS

- Requested quantities not exceeding dosing limits listed in Table 1.

APPROVAL LENGTH

- **Authorization:** 1 year.
- **Re-Authorization:** An updated letter of medical necessity or progress notes showing that current medical necessity criteria are met and that the medication is effective. NOTE: Lemtrada® will not be authorized for more than a total of 2 treatment courses.
    - All required drug safety monitoring for the requested medication listed in Table 1 has been completed.

APPENDIX

N/A

REFERENCES

1. A. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: Disease-modifying therapies for adults with multiple sclerosis: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology [published correction appears in Neurology. 2019 Jan 8;92(2):112]. *Neurology*. 2018;90(17):777-788. Accessed December 9, 2022. https://n.neurology.org/content/90/17/777.long#sec-4.
2. Aubagio. Prescribing information. Genzyme Corporation. 2022. Accessed December 9, 2022. http://products.sanofi.us/Aubagio/Aubagio.pdf.
3. Avonex. Prescribing information. Biogen Inc. 2021. Accessed December 9, 2022. https://www.avonex.com/content/dam/commercial/avonex/pat/en_us/pdf/Avonex_US_Prescribing_Information.pdf.
4. Copaxone. Prescribing information. Teva Pharmaceuticals. 2022. Accessed December 9, 2022. https://www.copaxone.com/globalassets/copaxone/prescribing-information.pdf.
5. Betaseron. Prescribing information. Bayer HealthCare Pharmaceuticals Inc. 2021. Accessed December 9, 2022. http://labeling.bayerhealthcare.com/html/products/pi/Betaseron_PI.pdf.
6. DynaMed. Multiple Sclerosis (MS). EBSCO Information Services. Accessed December 9, 2022. https://www.dynamed.com/condition/multiple-sclerosis-ms
7. Extavia. Prescribing information. Novartis Pharmaceuticals Corporation. 2021. Accessed December 9, 2022. https://www.novartis.us/sites/www.novartis.us/files/extavia.pdf.
8. Gilenya. Prescribing information. Novartis Pharmaceuticals Corporation. 2022. Accessed December 9, 2022. https://www.novartis.us/sites/www.novartis.us/files/gilenya.pdf.
9. Glatopa. Prescribing information. Sandoz Inc. 2022. Accessed December 9, 2022. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=5f01e40a-b6f6-40fb-b37c-3d06f1428e86.
10. Lemtrada. Prescribing information. Genzyme Corporation. 2022. Accessed December 9, 2022. http://products.sanofi.us/Lemtrada/Lemtrada.pdf.
11. Farez MF, Correale J, Armstrong MJ, et al. Practice guideline update summary: Vaccine-preventable infections and immunization in multiple sclerosis: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*. 2019;93(13):584-594. Accessed December 9, 2022. https://n.neurology.org/content/93/13/584.long.
12. Mavenclad. Prescribing information. EMD Serono Inc. 2022. Accessed December 9, 2022. https://www.emdserono.com/us-en/pi/mavenclad-pi.pdf.
13. Mayzent. Prescribing information. Novartis Pharmaceuticals Corporation. 2022. Accessed December 9, 2022. https://www.novartis.us/sites/www.novartis.us/files/mayzent.pdf.
14. National Multiple Sclerosis Society. Treating MS. Accessed December 9, 2022. https://www.nationalmssociety.org/Treating-MS.
15. Ocrevus. Prescribing information. Genetech Inc. 2022. Accessed December 9, 2022. https://www.gene.com/download/pdf/ocrevus_prescribing.pdf.

16. Plegridy. Prescribing information. Biogen Idec Inc. 2022. Accessed December 9, 2022. https://www.plegridy.com/content/dam/commercial/plegridy/pat/en_us/pdf/plegridy-prescribing-information.pdf.
17. Rebif. Prescribing information. EMD Serono Inc. 2021. Accessed December 9, 2022. http://www.emdserono.com/ms.country.us/en/images/Rebif_PI_tcm115_140051.pdf?Version=.
18. Tecfidera. Prescribing information. Biogen Inc. 2022. Accessed December 9, 2022. https://www.tecfidera.com/content/dam/commercial/tecfidera/pat/en_us/pdf/full-prescribing-info.pdf.
19. The use of Disease Modifying Therapies in Multiple Sclerosis. Accessed December 9, 2022. www.nationalmssociety.org/getmedia/5ca284d3-fc7c-4ba5-b005-ab537d495c3c/DMT_Consensus_MS_Coalition_color.%20Accessed%20Aug%2028%20,2017.
20. Tysabri. Prescribing information. Biogen Inc. 2021. Accessed December 9, 2022. https://www.tysabri.com/content/dam/commercial/tysabri/pat/en_us/pdf/tysabri_prescribing_information.pdf.
21. Vumerity. Prescribing information. Biogen Inc. 2022. Accessed December 9, 2022. https://www.vumerity.com/content/dam/commercial/vumerity/pat/en_us/pdf/vumerity-prescribing-information.pdf.
22. Zeposia. Prescribing information. Celgene Corporation. 2022. Accessed December 9, 2022. https://packageinserts.bms.com/pi/pi_zeposia.pdf.
23. Bafiertam. Prescribing information. Banner Life Sciences LLC. 2021. Accessed December 9, 2022. https://bafiertam.com/wp-content/uploads/2020/05/Bafiertam-Prescribing-Information-5-20-2020.pdf.
24. Kesimpta. Prescribing information. Novartis Pharmaceuticals. 2022. Accessed December 9, 2022. https://www.novartis.us/sites/www.novartis.us/files/kesimpta.pdf.
25. Ponvory. Prescribing information. Janssen Pharmaceuticals Inc. 2022. Accessed December 9, 2022. https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/PONVORY-pi.pdf.
26. Briumvi. Prescribing information. TG Therapeutics Inc. 2022. Accessed December 9, 2022. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761238s000lbl.pdf