Clinical Policy Title:	diroximel fumarate
Policy Number:	RxA.654
Drug(s) Applied:	Vumerity®
Original Policy Date:	09/14/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Diroximel fumarate (Vumerity®) is 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
diroximel fumarate (Vumerity®)	Relapsing multiple sclerosis	Starting dose: 231 mg twice daily, orally for 7 days; Maintenance dose after 7 days: 462 mg twice a day, orally.*	924 mg/day orally

*Vumerity® is not recommended in patients with moderate or severe renal impairment.

Dosage Forms

- Delayed-release capsules: 231 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Multiple Sclerosis (must meet all)**:**

1. Diagnosis of one of the following (a, b or c):
   a. Relapsing-remitting MS (RRMS);
   b. Secondary progressive MS (SPMS);
   c. Clinically isolated syndrome;
2. Prescribed by or in consultation with a neurologist;
3. Age ≥ 18 years;
4. Vumerity® is not prescribed concurrently with other disease modifying therapies for MS; (see Appendix B).
5. Does not exceed the following:
   a. Starting dose: 231 mg (administered as one 231 mg capsules) twice a day, orally for 7 days;

b. Maintenance dose After 7 days: 462 mg (administered as two 231 mg capsules) twice a day, orally.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Multiple Sclerosis (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Vumerity® is not prescribed concurrently with other disease modifying therapies for MS; (see Appendix B).
4. Does not exceed 462 mg (administered as two 231 mg capsules) twice a day, orally.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
CIS: Clinically isolated syndrome
FDA: Food and Drug Administration
MS: Multiple Sclerosis
RRMS: Relapsing-remitting multiple sclerosis
SPMS: Secondary progressive multiple sclerosis

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Infusion Therapies		
Tysabri®	300 mg intravenous every 4 weeks	300 mg/4 weeks
mitoxantrone	12 mg/m^2 given as a short (approximately 5 to 15 minutes) intravenous infusion every 3 months	Cumulative lifetime dose of ≥ 140 mg/m^2
Ocrevus®	Initial 300 mg intravenous infusion with a second 300 mg intravenous infusion two weeks later, followed by subsequent doses of 600 mg via intravenous infusion every 6 months	600 mg/6 months
Lemtrada®	intravenous infusion for 2 or more treatment courses: • First course: 12 mg/day on 5 consecutive days • Second course: 12 mg/day on 3 consecutive days 12 months after first course	See regimen

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	• Subsequent courses as needed: 12 mg/day on 3 consecutive days 12 months after any prior course	
Injectable therapies		
glatiramer (Copaxone®, Glatopa®)	20 mg subcutaneously once daily or 40 mg subcutaneously three times weekly	20 mg/day or 40 mg three times per week
Avonex®, Rebif®	Avonex®: 30 mcg IM weekly Rebif®: 22 mcg or 44 mcg subcutaneously three times weekly	Avonex®: 30 mcg/week Rebif®: 44 mcg three times per week
Betaseron®, Extavia®	250 mcg subcutaneously every other day	250 mg every other day
Plegridy®	Initially, give 63 mcg subcutaneously once on day 1. On day 15, increase the dose to 94 mcg subcutaneously once. On day 29, 125 mcg subcutaneously every 2 weeks. Continue with 125 mcg subcutaneously every 14 days thereafter.	125 mcg/2 weeks
Oral therapies		
Bafiertam™	Initial: 95 mg orally twice daily; after 7 days, increase to the maintenance dose of 190 mg orally twice daily.	380mg/day
Aubagio®	7 mg or 14 mg orally daily	14 mg/day
Gilenya™	0.5 mg orally daily	0.5 mg/day
dimethyl fumarate (Tecfidera®)	Initial: 120 mg orally twice daily; after 7 days, increase to the maintenance dose of 240 mg orally twice daily.	480 mg/day
Mayzent®	Day 1 and 2: 0.25 mg orally once daily Day 3: 0.5 mg orally once daily Day 4: 0.75 mg orally once daily For CYP2C9 genotypes *1/*1, *1/*2, or *2/*2: Day 5: 1.25 mg orally once daily Day 6 & onward: 2 mg orally once daily For CYP2C9 genotypes *1/*3 or *2/*3:	2 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Day 5 & onward: 1 mg orally once daily	
Zeposia®	Days 1-4: 0.23 mg orally once daily Days 5-7: 0.46 mg orally once daily Day 8 & onward: 0.92 mg orally once daily	0.92 mg/day
cladribine (Mavenclad®)	3.5 mg/kg over 2-year treatment course administered as 1.75 mg/kg in each year. Divide the 1.75 mg/kg dose over 2 cycles, each cycle lasting 4 to 5 consecutive days	20mg/day
dalfampridine (Ampyra®)	10 mg twice daily (approximately 12 hours apart)	20 mg/day

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Known hypersensitivity to diroximel fumarate, dimethyl fumarate, or to any of the excipients of Vumerity®;
  - Co-administration with dimethyl fumarate.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- Blood Tests Prior to Initiation of Vumerity®:
  - Obtain the following prior to treatment with Vumerity®:
    - A complete blood cell count (CBC), including lymphocyte count.
    - Serum aminotransferase, alkaline phosphatase, and total bilirubin levels.
- Swallow Vumerity® capsules whole and intact. Do not crush, chew, or sprinkle capsule contents on food.
- Avoid administration of Vumerity® with a high-fat, high-calorie meal/snack.
- Avoid co-administration of Vumerity® with alcohol.
- Pregnancy: Based on animal data, may cause fetal harm.
- Vumerity® is not recommended in patients with moderate or severe renal impairment.

References

1. Vumerity® Prescribing Information. Cambridge, MA; Biogen Inc.; January 2021. Available at: https://www.vumerityhcp.com/content/dam/commercial/vumerity/hcp/en_us/pdf/vumerity-prescribing-information.pdf. Accessed July 5, 2021.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: https://www.clinicalkey.com/pharmacology/. Accessed July 5, 2021.
3. 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. Neurology, 2018;90(17):777-788. doi:10.1212/WNL.0000000000005347. Available at: https://pubmed.ncbi.nlm.nih.gov/29686116/. Accessed July 5, 2021.
4. Rae-Grant A, Day GS, Marrie RA, et al. Comprehensive systematic review summary: Disease-modifying therapies for adults with multiple sclerosis Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology, 2018;90:789-800. doi:10.1212/WNL.0000000000005345. Available at: https://pubmed.ncbi.nlm.nih.gov/29686117/. Accessed July 5, 2021.
5. Costello K, Kalb R. The use of disease-modifying therapies in multiple sclerosis, principles and current evidence - a consensus paper by the Multiple Sclerosis Coalition. Revised September 2019. Available at http://www.nationalmssociety.org/getmedia/5ca284d3-fc7c- 4ba5-b005-ab537d495c3c/DMT_Consensus_MS_Coalition_color. Accessed July 5, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	08/2020	09/14/2020
Policy was reviewed: 1. Background was updated to include indication “Diroximel fumarate (Vumerity®) is indicated for the treatment…". 2. Dosing Information table was updated to remove extra information from indication and dosing regimen. And to update maximum dose from 462 mg twice a day to 924 mg/day. 3. Dosing Information was updated to include recommendation for severe renal impairment. 4. Dosage Form was updated to remove "For oral administration...". 5. Statement about provider sample "The provision of provider samples does not guarantee coverage…" was included to Clinical Policy. 6. Initial Approval Criteria I.A.2 was updated to remove trial and failure criteria, “Trial and failure of at least 2 preferred disease modifying therapies, at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;”. 7. Initial Approval Criteria I.A.6 was updated to split initial and maintenance dose. 8. Continuation Approval Criteria II.A.4 was updated to rephrase maximum dose criteria.	07/05/2021	09/14/2021

9. Initial and Continued Therapy Approval Criteria approval duration was updated to remove approval duration for HIM. 10. Appendix B was updated to include dosing regimen and maximum dose for all included drugs and to remove generic drugs natalizumab, ocrelizumab, alemtuzumab, interferon beta-1a, interferon beta-1b, peginterferon beta-1a, monomethyl fumarate, teriflunomide, fingolimod and siponimod as it was not available. 11. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 12. References were reviewed and updated.		