Clinical Policy Title:	monomethyl fumarate
Policy Number:	RxA.661
Drug(s) Applied:	Bafiertam™
Original Policy Date:	12/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Monomethyl fumarate (Bafiertam™) 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
monomethyl fumarate (Bafiertam™)	Relapsing MS	Starting: 95 mg PO BID for 7 days Maintenance: 190 mg PO BID	380 mg/day

Dosage Forms

- Delayed-release capsules: 95 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.

I. Initial Approval Criteria

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

1. Diagnosis of one of the following (a, b, or c):
   a. Clinically isolated syndrome;
   b. Relapsing-remitting Multiple Sclerosis;
   c. Secondary progressive Multiple Sclerosis;
2. Prescribed by or in consultation with a neurologist;
3. Age 18 years or older;
4. Monomethyl fumarate is not prescribed concurrently with other disease modifying therapies for MS (*see Appendix B*);
5. Dose does not exceed:
   a. Starting dose: 190 mg (2 capsules) per day for 7 days;
   b. Maintenance dose: 380 mg (4 capsules) per day.

Approval Duration
Commercial: 6 months

This clinical policy has been developed to authorize, modify, or determine coverage for individuals with similar conditions. Specific care and treatment may vary depending on individual need and benefits covered by the plan. This policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. This document may contain prescription brand name drugs that are trademarks of pharmaceutical manufacturers that are not affiliated with RxAdvance.

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Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving the 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. Monomethyl fumarate is not prescribed concurrently with other disease modifying therapies for MS;
4. If request is for a dose increase, new dose does not exceed 380 mg per day.

Approval Duration

Commercial: 12 months

Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
MS: Multiple Sclerosis
EDSS: Expanded Disability Status Scale
MRI: Magnetic Resonance Imaging
MMF: Monomethyl Fumarate
PML: Progressive Multifocal Leukoencephalopathy

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		
natalizumab (Tysabri®)	300 mg IV every 4 weeks	300 mg/4 weeks
mitoxantrone	12 mg/m^2 given as a short (approximately 5 to 15 minutes) IV infusion every 3 months	Cumulative lifetime dose of ≥ 140 mg/m^2
ocrelizumab (Ocrevus™)	Initial 300 mg IV infusion with a second 300 mg IV infusion two weeks later, followed by subsequent doses of 600 mg via IV infusion every 6 months	600 mg/6 months
alemtuzumab (Lemtrada®)	IV 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 • Subsequent courses as needed: 12 mg/day on 3 consecutive days 12 months after any prior course	See regimen

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Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Injectable therapies		
glatiramer (Copaxone®, Glatopa®)	20 mg SC once daily or 40 mg SC three times weekly	20 mg/day or 40 mg three times per week
interferon beta-1a (Avonex®, Rebif®)	Avonex®: 30 mcg IM weekly Rebif®: 22 mcg or 44 mcg SC three times weekly	Avonex®: 30 mcg/week Rebif®: 44 mcg three times per week
interferon beta-1b (Betaseron®, Extavia®)	250 mcg SC every other day	250 mg every other day
peginterferon beta-1a (Plegridy®)	125 mcg SC every 2 weeks	125 mcg/2 weeks
Oral therapies		
monomethyl fumarate (Bafiertam™)	Initial: 95 mg PO twice daily; after 7 days, increase to the maintenance dose of 190 mg PO twice daily.	380mg/day
diroximel fumarate (Vumerity®)	Starting: 231 mg PO twice daily for 7 days Maintenance: 462 mg PO twice daily	924 mg/day
teriflunomide (Aubagio®)	7 mg or 14 mg PO daily	14 mg/day
fingolimod (Gilenya™)	0.5 mg PO daily	0.5 mg/day
siponimod (Mayzent®)	Day 1 and 2: 0.25 mg PO once daily Day 3: 0.5 mg PO once daily Day 4: 0.75 mg PO once daily For CYP2C9 genotypes *1/*1, *1/*2, or *2/*2: Day 5: 1.25 mg PO once daily Day 6 & onward: 2 mg PO once daily For CYP2C9 genotypes *1/*3 or *2/*3: Day 5 & onward: 1 mg PO once daily	2 mg/day
ozanimod (Zeposia®)	Days 1-4: 0.23 mg PO once daily Days 5-7: 0.46 mg PO once daily Day 8 & onward: 0.92 mg PO 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 PO twice daily (approximately 12 hours apart)	20 mg/day

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

APPENDIX C: Contraindications/Boxed Warnings

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

- Boxed Warning(s):
  - None

APPENDIX D: General Information

- Most common adverse reactions are flushing, abdominal pain, diarrhea, and nausea. Allergic reactions, PML (progressive multifocal leukoencephalopathy), herpes zoster and other serious opportunistic infections, decreases in white blood cell counts, and liver injury, are among the potential serious adverse events that could occur.
- The American Academy of Neurology 2018 MS guidelines recommend the use of fingolimod, natalizumab and alemtuzumab for patients with highly active MS. Definitions of highly active MS vary and can include measures of relapsing activity and MRI markers of disease activity, such as numbers of gadolinium-enhanced lesions.
- The mechanism by which monomethyl fumarate exerts its therapeutic effect on MS is unknown. Monomethyl fumarate has been shown to activate the nuclear factor (erythroid-derived 2)-like 2 (Nrf2) pathway in vitro and in vivo in animals and humans. The Nrf2 pathway is involved in the cellular response to oxidative stress. MMF has been identified as a nicotinic acid receptor agonist in vitro.
- Monomethyl fumarate is a bioequivalent alternative to dimethyl fumarate and its prodrug.

References

1. Bafiertam™ Prescribing Information. High Point, NC: Banner Life Sciences LLC; April 2020. Available at: https://bafiertam.com/wp-content/uploads/2020/05/Bafiertam-Prescribing-Information-5-20-2020.pdf. Accessed May 27, 2021.
2. Banner Receives Tentative Approval for Bafiertam™ for the Treatment of Relapsing Forms of Multiple Sclerosis. Published January 2, 2019. Available at: https://www.businesswire.com/news/home/20190102005088/en/Banner-Receives-FDA-Tentative-Approval-Bafiertam-Treatment. Accessed May 27, 2021.
3. Multiple Sclerosis Association of America: Bafiertam™ Oral Capsules Approved by the FDA for Relapsing Forms of MS. Available at: https://mymsaa.org/news/bafiertam-oral-capsules-approved-by-the-fda-for-relapsing-forms-of-ms/. Accessed May 27, 2021.
4. 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. Full guideline available at: https://www.aan.com/Guidelines/home/GetGuidelineContent/904. Accessed May 27, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	09/24/2020	12/07/2020
Policy was reviewed:	5/27/21	6/10/21

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1. Clinical policy title was updated. 2. References were reviewed and updated.		

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