

Clinical Policy: Dimethyl Fumarate (Tecfidera), Diroximel Fumarate (Vumerity), Monomethyl Fumarate (Bafiertam)

Reference Number: CP.PCH.41

Effective Date: 02.01.21

Last Review Date: 05.22

Line of Business: Commercial, HIM

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

The following are nuclear factor-like 2 activators requiring prior authorization: dimethyl fumarate (Tecfidera[®]), diroximel fumarate (Vumerity[®]), and monomethyl fumarate (Bafiertam[™]).

FDA Approved Indication(s)

Tecfidera, Vumerity, and Bafiertam are indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation[®] that Tecfidera, Vumerity, and Bafiertam are **medically necessary** when the following criteria are met:

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, and:
 - i. If request is for Vumerity or Bafiertam: Member is contraindicated to both, or has experienced clinically significant adverse effects to one, of the following at up to maximally indicated doses: an interferon-beta agent (Avonex[®], Betaseron[®]/Extavia^{®†}, Rebif[®], or Plegridy[®]), glatiramer (Copaxone[®], Glatopa[®]);
 - b. Relapsing-remitting MS, and:
 - i. If request is for Vumerity or Bafiertam: Failure of all of the following at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated (1, 2, 3, and 4):*
 - 1) Dimethyl fumarate (generic Tecfidera);
 - 2) Aubagio[®];
 - 3) Gilenya[®];
 - 4) An interferon-beta agent (Avonex, Betaseron/Extavia[†], Rebif, or Plegridy) or glatiramer (Copaxone, Glatopa);

**Prior authorization is required for all disease modifying therapies for MS*

†Betaseron is the preferred interferon beta-1b product for the Commercial and HIM lines of business

- c. Secondary progressive MS;
- 2. Prescribed by or in consultation with a neurologist;
- 3. Age \geq 18 years;
- 4. For brand Tecfidera requests, member must use generic dimethyl fumarate, unless contraindicated or clinically significant adverse effects are experienced;
- 5. The requested agent is not prescribed concurrently with other disease modifying therapies for MS (*see Appendix D*);
- 6. Documentation of baseline number of relapses per year and expanded disability status scale (EDSS) score;
- 7. Dose does not exceed:
 - a. Starting dose: Tecfidera 240 mg (2 capsules) or Vumerity 462 mg (2 capsules) or Bafiertam 190 mg (2 capsules) per day for 7 days;
 - b. Maintenance dose: Tecfidera 480 mg (2 capsules) or Vumerity 924 mg (4 capsules) or Bafiertam 380 mg (4 capsules) per day.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2):

- 1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and HIM.PA.33 for health insurance marketplace; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and HIM.PA.103 for health insurance marketplace; or
- 2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial and HIM.PA.154 for health insurance marketplace.

II. Continued Therapy

A. Multiple Sclerosis (must meet all):

- 1. Member meets one of the following (a or b):
 - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
 - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
- 2. Member meets one of the following (a or b):
 - a. If member has received < 1 year of total treatment: Member is responding positively to therapy;

- b. If member has received ≥ 1 year of total treatment: Member meets one of the following (i, ii, iii, or iv):
 - i. Member has not had an increase in the number of relapses per year compared to baseline;
 - ii. Member has not had ≥ 2 new MRI-detected lesions;
 - iii. Member has not had an increase in EDSS score from baseline;
 - iv. Medical justification supports that member is responding positively to therapy;
 3. For brand Tecfidera requests, member must use generic dimethyl fumarate, unless contraindicated or clinically significant adverse effects are experienced;
 4. The requested agent is not prescribed concurrently with other disease modifying therapies for MS (*see Appendix D*);
 5. If request is for a dose increase, new dose does not exceed Tecfidera 480 mg (2 capsules) or Vumerity 924 mg (4 capsules) or Bafiertam 380 mg (4 capsules) per day.

Approval duration: first re-authorization: 6 months; second and subsequent re-authorizations: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and HIM.PA.33 for health insurance marketplace; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and HIM.PA.103 for health insurance marketplace; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial and HIM.PA.154 for health insurance marketplace.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial and HIM.PA.154 for health insurance marketplace or evidence of coverage documents;
- B.** Primary progressive MS.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

EDSS: expanded disability status scale

FDA: Food and Drug Administration

MS: multiple sclerosis

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Aubagio [®] (teriflunomide)	7 mg or 14 mg PO QD	14 mg/day
Avonex [®] , Rebif [®] (interferon beta-1a)	<i>Avonex</i> : 30 mcg IM Q week <i>Rebif</i> : 22 mcg or 44 mcg SC TIW	<i>Avonex</i> : 30 mcg/week <i>Rebif</i> : 44 mcg TIW
Betaseron [®] , Extavia [®] (interferon beta-1b)	250 mcg SC QOD	250 mg QOD
Plegridy [®] (peginterferon beta-1a)	125 mcg SC Q2 weeks	125 mcg/2 weeks
glatiramer acetate (Copaxone [®] , Glatopa [®])	20 mg SC QD or 40 mg SC TIW	20 mg/day or 40 mg TIW
Gilenya [®] (fingolimod)	0.5 mg PO QD	0.5 mg/day
dimethyl fumarate (Tecfidera [®])	120 mg PO BID for 7 days, followed by 240 mg PO BID	480 mg/day

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 dimethyl fumarate, diroximel fumarate, or any of the excipients of Tecfidera, Vumerity, or Bafiertam; coadministration of Tecfidera, Vumerity, and Bafiertam
- Boxed warning(s): none reported

Appendix D: General Information

- Disease-modifying therapies for MS are: glatiramer acetate (Copaxone[®], Glatopa[®]), interferon beta-1a (Avonex[®], Rebif[®]), interferon beta-1b (Betaseron[®], Extavia[®]), peginterferon beta-1a (Plegridy[®]), dimethyl fumarate (Tecfidera[®]), diroximel fumarate (Vumerity[®]), monomethyl fumarate (Bafiertam[™]), fingolimod (Gilenya[®], Tascenso ODT[™]), teriflunomide (Aubagio[®]), alemtuzumab (Lemtrada[®]), mitoxantrone (Novantrone[®]), natalizumab (Tysabri[®]), ocrelizumab (Ocrevus[®]), cladribine (Mavenclad[®]), siponimod (Mayzent[®]), ozanimod (Zeposia[®]), ponesimod (Ponvory[™]), and ofatumumab (Kesimpta[®]).
- Of the disease-modifying therapies for MS that are FDA-labeled for CIS, only the interferon products, glatiramer, and Aubagio have demonstrated any efficacy in decreasing the risk of conversion to MS compared to placebo. This is supported by the American Academy of Neurology 2018 MS guidelines.
- Tecfidera and Vumerity are both prodrugs of Bafiertam.

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Dimethyl fumarate (Tecfidera)	Starting: 120 mg PO BID for 7 days Maintenance: 240 mg PO BID	480 mg/day
Diroximel fumarate (Vumerity)	Starting: 231 mg PO BID for 7 days Maintenance: 462 mg PO BID	924 mg/day
Monomethyl fumarate (Bafiertam)	Starting: 95 mg PO BID for 7 days Maintenance: 190 mg PO BID	380 mg/day

VI. Product Availability

Drug Name	Availability
Dimethyl fumarate (Tecfidera)	Delayed-release capsules: 120 mg, 240 mg
Diroximel fumarate (Vumerity)	Delayed-release capsule: 231 mg
Monomethyl fumarate (Bafiertam)	Delayed-release capsule: 95 mg

VII. References

1. Tecfidera Prescribing Information. Cambridge, MA: Biogen Inc.; January 2021. Available at <http://www.tecfidera.com>. Accessed February 4, 2022.
2. Vumerity Prescribing Information. Cambridge, MA: Biogen Inc.; January 2021. Available at <http://www.vumerity.com>. Accessed February 4, 2022.
3. Bafiertam Prescribing Information. High Point, NC: Banner Life Sciences LLC; May 2021. Available at: <https://bafiertam.com/prescribing-information>. Accessed February 7, 2022.
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>.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created (Commercial and HIM line of business separated from CP.PHAR.249). Per November and December SDC and prior clinical guidance, removed redirection to Mayzent; for RRMS modified redirection for Vumerity requests to require generic dimethyl fumarate, Aubagio, Gilenya, and either an interferon-beta agent or glatiramer; clarified requirement for medical justification why generic dimethyl fumarate cannot be used applies only to brand Tecfidera requests.	01.11.21	02.21
2Q 2021 annual review: added Bafiertam (CP.PHAR.460 retired); revised medical justification language to require use of the generic product; references reviewed and updated.	02.08.21	05.21
2Q 2022 annual review: no significant changes; clarified interferon-beta product redirections for each line of business per SDC; references reviewed and updated.	02.07.22	05.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Template changes applied to other diagnoses/indications and continued therapy section.	09.29.22	
Added generic redirection for continued therapy section.	12.15.22	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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