# Drug and Biologic Coverage Policy

**Effective Date** ........................................... 1/1/2022  
**Next Review Date** ........................................ 1/1/2023  
**Coverage Policy Number** ............................... IP0266

## Dimethyl fumarate

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### Related Coverage Resources

**INSTRUCTIONS FOR USE**

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer’s particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer’s benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer’s benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

### Overview

This policy supports medical necessity review for the following dimethyl fumarate products:

- **Dimethyl fumarate** delayed-release capsules
- **Tecfidera®** (dimethyl fumarate) delayed-release capsules

### Medical Necessity Criteria

Dimethyl fumarate (Tecfidera) is considered medically necessary when the following are met:

1. **Multiple Sclerosis.** Individual meets the following criteria:
   A. Documented diagnosis of **ONE** of the following:
      i. Active Secondary Progressive Multiple Sclerosis (SPMS) (for example, SPMS with a documented relapse)
      ii. Clinically Isolated Syndrome
      iii. Relapsing-Remitting Multiple Sclerosis
Coverage for Dimethyl fumarate (Tecfidera) varies across plans and may require the use of preferred products in addition to the medical necessity criteria listed above. Refer to the customer’s benefit plan document for coverage details.

When coverage requires the use of preferred products, there is documentation of ONE of the following:

A. The individual has had inadequate efficacy to the number of covered alternatives according to the table below

OR

B. The individual has a contraindication according to FDA label, significant intolerance, or is not a candidate* for the covered alternatives according to the table below

*Note: Not a candidate due to being subject to a warning per the prescribing information (labeling), having a disease characteristic, individual clinical factor[s], other attributes/conditions, or is unable to administer and requires this dosage formulation)

Step Therapy Requirements by Drug List:

<table>
<thead>
<tr>
<th>Product</th>
<th>Standard / Performance</th>
<th>Value / Advantage</th>
<th>Cigna Total Savings</th>
<th>Legacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tecfidera (dimethyl fumarate)</td>
<td>• Dimethyl fumarate (generic for Tecfidera)*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Documentation that individual has tried the bioequivalent generic product AND cannot take due to a formulation difference in the inactive ingredient(s) [for example, difference in dyes, fillers, preservatives] between the brand and the bioequivalent generic product which, per the prescribing physician, would result in a significant allergy or serious adverse reaction

Individual and Family Plan Preferred Alternative(s):

<table>
<thead>
<tr>
<th>Product</th>
<th>Covered Alternative(s)</th>
</tr>
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*Documentation that individual has tried the bioequivalent generic product AND cannot take due to a formulation difference in the inactive ingredient(s) [for example, difference in dyes, fillers, preservatives] between the brand and the bioequivalent generic product which, per the prescribing physician, would result in a significant allergy or serious adverse reaction.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Note: Receipt of sample product does not satisfy any criteria requirements for coverage.

Reauthorization Criteria

Dimethyl fumarate (Tecfidera) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration is up to 12 months.

Reauthorization approval duration is up to 12 months.

Conditions Not Covered

Dimethyl fumarate (Tecfidera) is considered experimental, investigational or unproven for ANY other use including the following (this list may not be all inclusive):
1. Concurrent Use with Other Disease-Modifying Agents Used for Multiple Sclerosis.  Note: Examples of disease modifying agents used for multiple sclerosis include Aubagio® (teriflunomide tablets), Avonex® (interferon beta 1a injection [intramuscular]), Betaseron®/Extavia® (interferon beta-1b injection), Rebif® (interferon beta-1a injection [subcutaneous]), Copaxone®/Glatopa® (glatiramer acetate injection), Plegridy® (peginterferon beta-1a injection), Gilenya® (fingolimod tablets), Mavenclad® (cladribine tablets), Mayzent® (siponimod tablets), Bafiertam® (monomethyl fumarate delayed-release capsules), Vumerity® (diroximel fumarate delayed-release capsules), Zeposia® (ozanimod capsules), Ocrevus® (ocrelizumab injection for intravenous use), Tysabri® (natalizumab injection for intravenous infusion), Lemtrada® (alemtuzumab injection for intravenous use), and Kesimpta® (ofatumumab injection for subcutaneous use).  These agents are not indicated for use in combination.  Additional data are required to determine if use of disease-modifying multiple sclerosis agents in combination is safe and provides added efficacy.

2. Non-Relapsing Forms of Multiple Sclerosis.  
   Note: An example of a non-relapsing form of multiple sclerosis is primary progressive multiple sclerosis.  The efficacy of dimethyl fumarate has not been established in patients with multiple sclerosis with non-relapsing forms of multiple sclerosis.  

Background

OVERVIEW
Dimethyl fumarate is 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 MS in adults.  

Disease Overview
MS is a chronic, inflammatory, demyelinating, autoimmune disease of the central nervous system (CNS) that impacts almost 1,000,000 people in the US.  The condition is marked by inflammation and demyelination, as well as degenerative alterations.  Patients usually experience relapses and remissions in their neurological symptoms.  For most patients, the onset of MS symptoms occurs when patients are 20 to 40 years of age; however, children can get MS and new onset disease can occur in older adults.  The MS disease course is heterogeneous but has some patterns.  Approximately 85% to 90% of patients have a relapsing pattern at onset.  However, this transitions over time in patients who are untreated to a worsening with very few or no relapses or magnetic resonance imaging (MRI) activity (secondary progressive MS).  Around 10% to 15% of patients have a steady progression of symptoms over time (primary progressive MS), marked by some clinical manifestations or by MRI activity.  Primary progressive MS is generally diagnosed in patients on the upper level of the typical age range (e.g., almost 40 years of age) and the distribution is equivalent among the two genders.  Advances in the understanding of the MS disease process, as well as in MRI technology, spurred updated disease course descriptions in 2013, as well as in 2017.  The revised disease courses are clinically isolated syndrome, relapsing remitting MS, primary progressive MS, and secondary progressive MS.  Clinically isolated syndrome is now more recognized among the course descriptions of MS.  It is the first clinical presentation of MS that displays characteristics of inflammatory demyelination that may possibly be MS but has yet to fulfill diagnostic criteria.  It is notable that the other MS designations can be further characterized considering whether patients have active disease (or not active), as well as if disease is worsening or stable.  Disability in MS is commonly graded on the deterioration of mobility per the Expanded Disability Status Scale (EDSS) an ordinal scale that ranges from 0 to 10, with higher scores indicating greater disability.  

Guidelines
In September 2019, a consensus paper was updated by the MS Coalition that discusses the use of disease-modifying therapies in MS.  Many options from various disease classes, involving different mechanisms of action and modes of administration, have shown benefits in patients with MS.  

Safety
Progressive multifocal leukoencephalopathy has occurred in patients with MS treated with dimethyl fumarate, including a fatal case.
References


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