Tecfidera (dimethyl fumarate)
Policy Number: C3891-A

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DATE
5/1/2018	2/12/2020	2/12/2021
J CODE	**TYPE OF CRITERIA**	**LAST P&T APPROVAL/VERSION**
J8499 (NOC)	RxPA	Q2 2020 20200422C3891-A

PRODUCTS AFFECTED:
Tecfidera (dimethyl fumarate)

DRUG CLASS:
Multiple Sclerosis Agents - Nrf2 Pathway Activators

ROUTE OF ADMINISTRATION:
Oral

PLACE OF SERVICE:
Specialty Pharmacy

AVAILABLE DOSAGE FORMS:
Tecfidera MISC 120 & 240MG, Tecfidera CPDR 120MG, Tecfidera CPDR 240MG
30-day Starter Pack, (NDC 64406-007-03): 7-day bottle 120 mg capsules, quantity 14, 23-day bottle 240 mg capsules, quantity 46
120 mg capsules: 7-day bottle of 14 capsules (NDC 64406-005-01)
240 mg capsules: 30-day bottle of 60 capsules (NDC 64406-006-02)

FDA-APPROVED USES:
Indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS)

COMPENDIAL APPROVED OFF-LABELED USES:
None

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS:
Multiple Sclerosis

REQUIRED MEDICAL INFORMATION:
A. RELAPSING FORM OF MULTIPLE SCLEROSIS:
1. Documentation of a definitive diagnosis of a relapsing form of multiple sclerosis as defined by the McDonald criteria (see Appendix), including: Relapsing- remitting multiple sclerosis [RRMS], secondary-progressive multiple sclerosis [SPMS] with relapses, and progressive-relapsing multiple sclerosis [PRMS] or First clinical episode with MRI features consistent with multiple sclerosis
AND
2. Member is not currently being treated with a disease-modifying agent (DMA) other than the requested agent

AND

3. Documentation of a complete blood cell count (CBC), including lymphocyte count and liver enzyme laboratory testing was completed, reviewed, and deemed appropriate for Tecfidara treatment by the prescriber
AND
4. IF REQUEST IS FOR A NON-FORMULARY PRODUCT: Documentation of trial/failure of or intolerance to a majority (not more than 3) of the preferred formulary/PDL alternatives for the given diagnosis. If yes, please submit documentation including medication(s) tried, dates of trial(s) and reason for treatment failure(s).

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of therapy: 12 months

QUANTITY:
maximum dose of 240mg twice daily

PRESCRIBER REQUIREMENTS:
Prescribed by, or in consultation with, a board certified neurologist or a multiple sclerosis specialist. Submit consultation notes if applicable

AGE RESTRICTIONS:
18 years of age and older

CONTINUATION OF THERAPY:
A. RELAPSING FORM OF MULTIPLE SCLEROSIS:
1. (a) Documentation of a stable number or decrease in acute attacks (relapses) within the last 6 months
OR
(b) Documentation of lack of progression or sustained disability
OR
(c) Recent (within last 6 months) MRI shows lack of development of new asymptomatic lesions
AND
2. Documentation member has been adherent to therapy at least 85% of the time as verified by Prescriber and member's medication fill history
AND
3. Member had not experienced any intolerable adverse effects or drug toxicity
AND
4. Documentation of an updated complete blood cell count (CBC) and liver enzyme laboratory test [Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and total bilirubin] since initial authorization was completed, reviewed, and deemed appropriate for Tecfidara treatment by the prescriber

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Tecfidera (dimethyl fumarate) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Concurrent use with other disease-modifying agents used for MS.

OTHER SPECIAL CONSIDERATIONS:
None

BACKGROUND:

Tecfidera™ (dimethyl fumarate, DMF) is indicated for the treatment of patients with relapsing forms of multiple sclerosis. The mechanism by which DMF exerts its therapeutic effect in multiple sclerosis is unknown. DMF and its active metabolite, monomethyl fumarate (MMF), have been shown to activate the Nuclear factor (erythroidderived 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. DMF and MMF are postulated to decrease oxidative stress and protect axons from inflammatory mediators. MS is a chronic autoimmune disorder of the central nervous system (CNS) in which white blood cells (WBCs) attack and damage the myelin sheath of nerve cells in the CNS. This damage disrupts transmission of nerve impulses. Damage occurs in areas of the brain, spinal cord, and optic nerves. The damage ultimately leads to progressive physical and cognitive disabilities. The clinical course of MS is highly variable. There are four recognized clinical forms: relapsing remitting (RRMS), secondary progressive (SPMS), primary progressive (PPMS), and progressive relapsing (PRMS). RRMS is the most common form of the disease. Because MS can affect any area of the brain, optic nerve, or spinal cord, MS can cause almost any neurologic symptom. Patients often present as young adults with 2 or more clinically distinct episodes of CNS dysfunction with at least partial resolution. Episodes involve numbness, weakness, or incoordination affecting an arm, a leg, or both. Additional symptoms include pain, vertigo, cognitive deficits (such as impaired memory, attention, or judgment), fatigue, speech deficits (such as dysarthria or less commonly aphasia), and bowel, bladder, and sexual dysfunction. The pathological hallmark of MS is the cerebral or spinal plaque on magnetic resonance imaging (MRI). Plaques are discrete regions of demyelination with relative preservation of axons. The neurologic history and physical examination help establish the diagnosis of MS. Diagnostic criteria are symptoms and signs disseminated in time and space (i.e., more than one episode involving more than one area of the CNS). These criteria have been largely replaced by the McDonald criteria, developed in 2001 by the International Panel on the Diagnosis of Multiple Sclerosis. The McDonald criteria retain many features of the original criteria and are intended for use in both clinical practice and clinical trial settings. Diagnoses of “definite MS,” “possible MS,” or, if there is a better explanation for the clinical presentation, “not MS” are determined by findings on clinical exam, MRI, cerebrospinal fluid, and visual evoked potentials. The term “clinically isolated syndrome” (CIS) describes patients who have suffered a first clinical attack but do not meet diagnostic criteria for definite MS. The most recent update in 2010 allows the diagnosis of MS in some patients with CIS.

APPENDIX:

Summary of 2017 McDonald Criteria for the Diagnosis of MS

CLINICAL PRESENTATION	ADDITIONAL CRITERIA TO MAKE MS DIAGNOSIS
...in a person who has experienced a typical attack/CIS at onset	
• 2 or more attacks and clinical evidence of 2 or more lesions; OR • 2 or more attacks and clinical evidence of 1 lesion with clear historical evidence of prior attack involving lesion in different location	None. DIS and DIT have been met.
• 2 or more attacks and clinical evidence of 1 lesion	DIS shown by <u>one</u> of these criteria: - additional clinical attack implicating different CNS site - 1 or more MS-typical T2 lesions in 2 or more areas of CNS: periventricular, cortical, juxtacortical, infratentorial or spinal cord
• 1 attack and clinical evidence of 2 or more lesions	DIT shown by <u>one</u> of these criteria: - Additional clinical attack - Simultaneous presence of both enhancing and non-enhancing MS-typical MRI lesions, or new T2 or enhancing MRI lesion compared to baseline scan (without regard to timing of baseline scan) - CSF oligoclonal bands
• 1 attack and clinical evidence of 1 lesion	DIS shown by <u>one</u> of these criteria: - Additional attack implicating different CNS site - 1 or more MS-typical T2 lesions in 2 or more areas of CNS: periventricular, cortical, juxtacortical, infratentorial or spinal cord **AND** DIT shown by <u>one</u> of these criteria: - additional clinical attack - Simultaneous presence of both enhancing and non-enhancing MS-typical MRI lesions, or new T2 or enhancing MRI lesion compared to baseline scan (without regard to timing of baseline scan) - CSF oligoclonal bands
...in a person who has steady progression of disease since onset	
1 year of disease progression (retrospective or prospective)	DIS shown by at least <u>two</u> of these criteria: - 1 or more MS-typical T2 lesions (periventricular, cortical, juxtacortical or infratentorial) - 2 or more T2 spinal cord lesions - CSF oligoclonal bands

DIT = Dissemination in time **CNS** = central nervous system **CSF** = cerebrospinal fluid
DIS = Dissemination in space **T2 lesion** = hyperintense lesion on T2-weighted MRI

Documentation Requirements:

Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

REFERENCES:

1. Tecfidera (dimethyl fumarate) [prescribing information]. Cambridge, MA: Biogen Idec Inc; July 2019.
2. 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.
3. Thompson, A., Banwell, B. et al. (2018). Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. The Lancet Neurology, 17(2), pp.162-173.