Vumerity (diroximel fumarate)
Policy Number: C17992-A

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DATE
02/01/2020	12/19/2019	12/19/2020
J CODE	**TYPE OF CRITERIA**	**LAST P&T APPROVAL/VERSION**
NA	RxPA	Q1 2020 20200122C17992-A

PRODUCTS AFFECTED:
Vumerity (diroximel fumarate)

DRUG CLASS:
Multiple Sclerosis Agents - Nrf2 Pathway Activators

ROUTE OF ADMINISTRATION:
Oral

PLACE OF SERVICE:
Specialty Pharmacy

AVAILABLE DOSAGE FORMS:
Vumerity (Starter) CPDR 231MG (diroximel fumarate Capsule DR Starter Bottle 231 MG (bottle= 106), Vumerity CPDR 231MG (diroximel fumarate)- (bottle= 120)

FDA-APPROVED USES:
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

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. The 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 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:
Starting dose: 231 mg twice a day, orally, for 7 days, Maintenance dose after 7 days: 462 mg (administered as two 231 mg capsules) twice a day, orally

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a board-certified neurologist or a multiple sclerosis specialist. Please submit consultation notes if prescribed after consultation

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 since initial authorization was completed, reviewed, and deemed appropriate for treatment by the prescriber

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Vumerity (diroximel fumarate) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy.

OTHER SPECIAL CONSIDERATIONS:
None

BACKGROUND:
Vumerity: Key Studies for Approval
The efficacy of Vumerity is based upon bioavailability studies in patients with relapsing forms of MS and healthy subjects comparing Tecfidera to Vumerity. After oral administration of Vumerity, diroximel

rapid presystemic hydrolysis by esterases and is converted to its active metabolite, monomethyl fumarate (MMF). Diroximel fumarate is not quantifiable in plasma following oral administration of Vumerity. Therefore, all pharmacokinetic analyses related to Vumerity were performed with plasma MMF

concentrations. Pharmacokinetic data were obtained in subjects with relapsing forms of multiple sclerosis (MS) and healthy volunteers. All bioavailability studies met their endpoints. The key study for Biogen in providing differentiation from Tecfidera is the EVOLVE-MS-2 study. In July 2019, Biogen announced positive results from EVOLVE-MS-2, a randomized, double-blind, five-week, Phase 3 study of diroximel fumarate compared to Tecfidera. According to the company's press release, diroximel fumarate was statistically superior to dimethyl fumarate on the study's pre-specified primary endpoint, with patients treated with diroximel fumarate self-reporting significantly fewer days of key gastrointestinal (GI) symptoms with intensity scores ≥2 on the Individual Gastrointestinal Symptom and Impact Scale (IGISIS), as compared to dimethyl fumarate (p=0.0003). The most common adverse events (AEs) reported in the study for both treatment groups were flushing, diarrhea and nausea (32.8%, 15.4%, and 14.6% for diroximel fumarate; 40.6%, 22.3%, and 20.7% for dimethyl fumarate). The overall proportion of patients with AEs leading to study discontinuation were 1.6% for diroximel fumarate and 6.0% for dimethyl fumarate. Of those, the proportion of patients who discontinued due to GI adverse events during the five-week treatment period were 0.8% for diroximel fumarate and 4.8% for dimethyl fumarate.

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 one 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 one 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 one 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 one 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 two 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
DIS = Dissemination in space
CNS = central nervous system
T2 lesion = hyperintense lesion on T2-weighted MRI
CSF = cerebrospinal fluid

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