Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 08/08/2024

Ohtuvayre™ (ensifentrine)

HCPCS: J7699

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Trial and failure of dual therapy with a long-acting beta-2 agonist (LABA) and long-acting muscarinic antagonist (LAMA)
   d. Trial and failure, contraindication, or intolerance to the preferred drugs as listed in BCBSM/BCN's prior authorization and step therapy documents

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: One year at a time
   c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit.

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Ohtuvayre is a phosphodiesterase-3 (PDE3) inhibitor and phosphodiesterase-4 (PDE4) inhibitor indicated for the maintenance treatment of chronic obstructive pulmonary disease (COPD) in adult patients.

- The 2024 Global Initiative for Chronic Obstructive Lung Disease (GOLD) Report ("GOLD guideline") defines COPD as a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, sputum production, and/or exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive airflow obstruction. As the definition states, COPD includes chronic bronchitis and/or emphysema, which both make emptying air from the lungs progressively more difficult. Most people with COPD have a combination of both conditions. Dyspnea is the most common symptom of COPD; however, chronic cough and sputum production are also cardinal symptoms. COPD is a common, chronic lung disease. It is estimated that 16 million people in the United States have COPD, which represents a prevalence of about 6% among adults. COPD is almost exclusively diagnosed in adulthood, typically in adults over the age of 40 years. However, factors/exposures from childhood (e.g. premature birth, respiratory infections, secondhand smoke) are thought to play a role in the future development of COPD in some patients. The prevalence of COPD increases with age, with an estimated prevalence of over 12% in the 65 years of age and older population. COPD is slightly more common in women than men.

- The GOLD guideline's (2024) initial treatment algorithm for COPD is individualized based on an assessment of the patient's symptoms and exacerbation history. These assessments determine the suggested treatment option for patients. Initial pharmacologic treatment includes either a bronchodilator, LABA + LAMA, or LABA + LAMA + inhaled corticosteroid (ICS) depending on a patient's symptoms and exacerbation history. If a patient's response to initial treatment is appropriate, they should be maintained on that treatment. If a patient does not respond to initial treatment, then adherence, inhaler technique, and possible interfering comorbidities should be checked. Follow-up pharmacologic treatment follows a stepwise approach and is determined based on whether dyspnea or exacerbations are the predominant treatable trait to target. If dyspnea is the predominant trait a patient should start with either a LAMA or LABA and should progress to LABA + LAMA. If exacerbations are the predominant trait then patients should start with a LABA or LAMA, progress to LABA + LAMA (+ICS if blood eosinophil count ≥ 300 cells/µL) and eventually add on roflumilast (if FEV1 <50% and chronic bronchitis) or add azithromycin (preferred in former smokers). The GOLD guidelines have not been updated to include Ohtuvayre at this time.

- The efficacy of Ohtuvayre was evaluated in two 24-week randomized, double-blind, placebo-controlled, parallel-group clinical trials (ENHANCE-1 and ENHANCE-2). The two trials enrolled a total of 1,553 adults with moderate to severe COPD with or without background LABA ± ICS or LAMA ± ICS maintenance therapy. Ohtuvayre was not studied as an add-on treatment to standard-of-care dual LAMA/LABA or triple LAMA/LABA/ICS inhaler maintenance therapies.

    - The primary endpoint for ENHANCE-1 and ENHANCE-2 was the change from baseline in FEV1 $AUC_{0\text{-}12h}$ post-dose at Week 12.

        - In ENHANCE-1 and ENHANCE-2, Ohtuvayre demonstrated an improvement in lung function, with an average increase in FEV1 $AUC_{0–12h}$ of 87 mL and 94 mL, respectively, versus placebo at Week 12 ($p < 0.001$).

    - In ENHANCE-1 and ENHANCE-2, an analysis was conducted to determine the effect of Ohtuvayre compared with placebo on the annual moderate to severe COPD exacerbation rate but was not part of the formal testing hierarchy.

        - Pooled analysis of the two studies also showed that Ohtuvayre reduced exacerbations through 24 weeks by 40% in patients with moderate to severe COPD.

References:

1. Ohtuvayre [prescribing information]. Raleigh, NC. Verona Pharma, Inc. June 2024.
2. IPD Analytics New Drug Preview – Ensifentrine (RPL554). December 2023. IPDAnalytics.com
3. Global Initiative for Chronic Obstructive Lung Disease – 2024 Report. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. December 2023. 2024 GOLD Report - Global Initiative for Chronic Obstructive Lung Disease - GOLD (goldcopd.org)

<table>
<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>1.1</td><td>Effective Date: 08/08/2024</td><td>New policy</td></tr>
<tr><td>1.0</td><td>Effective Date: 07/15/2024</td><td>UM medical management system update for MAPPO and BCNA
<table>
<tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr>
<tr><td>BCBS</td><td>No</td></tr>
<tr><td>BCN</td><td>No</td></tr>
<tr><td>MAPPO</td><td>Yes</td></tr>
<tr><td>BCNA</td><td>Yes</td></tr>
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form

Blue Cross Blue Shield Blue Care Network of Michigan

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This form is to be used by participating physicians to obtain coverage for **drugs covered under the medical benefit**. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	**Name**
ID Number	**Specialty**
D.O.B. ☐Male ☐Female	**Address**
Diagnosis	**City /State/Zip**
Drug Name	**Phone/Fax: P**: ( ) - **F**: ( ) -
Dose and Quantity	**NPI**
Directions	**Contact Person**
Date of Service(s)	**Contact Person Phone / Ext.**

STEP 1: DISEASE STATE INFORMATION

1. Is this request for: ☐ Initiation ☐ Continuation *Date patient started therapy:* _____
2. Administered by patient or a medical professional? ☐ patient (self) ☐ health care professional (physician, nurse, etc.)
3. Site of administration? ☐ Provider office/Home infusion ☐ Other: _____
   ☐ Hospital outpatient facility (go to #4) *Reason for Hospital Outpatient administration:* _____
   ☐ Hospital inpatient facility for Car-T therapy only (for example: Kymriah, Yescarta, or Tecartus) (go to #5)
4. Please specify location of administration if hospital outpatient infusion: _____
5. Please specify location of administration if hospital inpatient infusion: _____
6. Please provide the NPI number for the place of administration: _____
7. **Initiation AND Continuation of therapy:**
   a. What is the patient's diagnosis? _____
   b. What other medication has the patient received for their condition? Please list_____
      i. Please describe the response to previous therapies:
      _____
   c. Will the patient be receiving any other treatment for the listed condition while on this medication? Please list:
      _____
   d. Please list any labs values important for diagnosing or monitoring this patient's condition:
      _____
8. **Continuation of therapy:**
   a. Has the patient progressed while on this medication? ☐ yes ☐ no
   b. How has the patient's condition changed while on this medication?
      ☐ Improved: Please describe: _____
      ☐ Stable: please describe: _____
      ☐ Worsened; Please describe: _____
      ☐ Other; Please describe: _____

Chart notes are required for the processing of all requests. Please add any other supporting medical information necessary for our review **(required)**

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name **Physician Signature** **Date**

Step 2: Checklist	☐ Form Completely Filled Out ☐ Provide chart notes	☐ Attach test results
Step 3: Submit	**By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979**	**By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320**

7/26/2018, 9/18/2018; 1/31/2020; 3/17/2020; 8/9/2021