# Pharmacy Management Drug Policy

**SUBJECT: Ohtuvayre (ensifentrine)**
**POLICY NUMBER: PHARMACY-125**
**EFFECTIVE DATE: 01/2025**
**LAST REVIEW DATE: 02/12/2026**

*If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. This drug policy applies to the following line/s of business:*

**Policy Application**

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| **Category**: | ☒ Commercial Group (e.g., EPO, HMO, POS, PPO) | ☒ Medicare Advantage |
| | ☒ On Exchange Qualified Health Plans (QHP) | ☐ Medicare Part D |
| | ☒ Off Exchange Direct Pay | ☒ Essential Plan (EP) |
| | ☒ Medicaid & Health and Recovery Plans (MMC/HARP) | ☐ Child Health Plus (CHP) |
| | ☐ Federal Employee Program (FEP) | ☐ Ancillary Services |
| | ☒ Dual Eligible Special Needs Plan (D-SNP) | |

## DESCRIPTION:

Chronic obstructive pulmonary disease (COPD) is defined 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.[1] COPD includes both 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. The most common symptoms of COPD are dyspnea, chronic cough, and sputum production.

COPD is typically diagnosed in adulthood in those over the age of 40 years, with prevalence increasing with age. COPD results from gene-environment interactions occurring over the lifetime of the individual that can damage the lungs and/or alter their normal development/aging process.[1] The most common risk factor for COPD is tobacco smoking. However, additional risk factors include air pollution, occupational exposures, poorly controlled asthma, environmental tobacco smoke, infectious diseases, and low socioeconomic status.[2]

Diagnosis of COPD requires the presence of non-fully reversible airflow obstruction measured by spirometry ($FEV_1/FVC < 0.7$ post-bronchodilation).[1] The severity of the airflow obstruction is determined using the $FEV_1$ obtained from spirometry. The GOLD guidelines recommend the following cutoff points for determining severity:

- GOLD 1 (mild): $FEV_1 \geq 80\%$ predicted
- GOLD 2 (moderate): $50\% \leq FEV_1 < 80\%$ predicted
- GOLD 3 (severe): $30\% \leq FEV_1 < 50\%$ predicted
- GOLD 4 (very severe): $FEV_1 < 30\%$ predicted

Current treatments recommendations utilize the GOLD guideline's algorithm for pharmacologic treatment of COPD. Treatment recommendations are based upon the assessment of symptoms (using the modified Research Council (mMRC) dyspnea scale or the COPD Assessment Test (CAT) test) and the history of exacerbations. Initial treatment options include long-acting beta-2 agonists (LABA) or long-acting muscarinic antagonists, used alone, or in combination. Inhaled corticosteroids (ICS) may be added to LABA/LAMA dual therapy for those with continued exacerbations and an eosinophil count ≥ 300 cells/µL. Additional add-on therapies for those with continued exacerbations

may include roflumilast (a PDE-4 inhibitor), maintenance azithromycin treatment, or dupilumab (for those with blood eosinophils ≥ 300 cells/µL).

Ohtuvayre (ensifentrine) is indicated for the maintenance treatment of COPD in adult patients. Ohtuvayre is a combination phosphodiesterase 3 (PDE3) inhibitor and phosphodiesterase 4 (PDE4) inhibitor. The recommended dosage of Ohtuvayre is 3 mg (one unit-dose ampule) twice daily, once in the morning and once in the evening, administered by oral inhalation using a standard jet nebulizer with a mouthpiece.

The approval of Ohtuvayre was supported by data from the ENHANCE-1 and ENHANCE-2 phase 3 trials evaluating the safety and efficacy of ensifentrine in moderate-to severe COPD patients stable on background therapy (including no therapy, or LAMA or LABA, with or without ICS) over 24 weeks. The primary efficacy endpoint was the mean change from baseline to Week 12 in the $FEV_1$ area under the concentration-time curve over 12 hours. Ensifentrine demonstrated an improvement of lung function, with an average increase in $FEV_1AUC_{0\text{-}12\ h}$ of 87 mL and 94 mL, respectively, versus placebo at week 12. However, patients receiving standard of care dual LAMA/LABA or triple LAMA/LABA/ICS therapy were excluded from the trial. In addition, 38.2% of patients were on no background therapy.

**POLICY:**

| **Ohtuvayre (ensifentrine) – Rx and Medical** |
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| **Ohtuvayre is covered as an Rx benefit ONLY for the Commercial/Exchange/SafetyNet Plans.**<br><br>1. Must be requested by, or in consultation with, a pulmonologist **AND**<br>2. Must be 18 years of age or older **AND**<br>3. Must have confirmed diagnosis of COPD by spirometry documenting $FEV_1$/FVC ratio < 0.7 post-bronchodilation **AND**<br>4. Must have moderate to severe disease<br>a. Moderate to severe disease defined as GOLD 2 (moderate) or GOLD 3 (severe) airflow obstruction as demonstrated by 30% ≤ $FEV_1$ < 80% predicted **AND**<br>5. Must be symptomatic, defined as ONE of the following:<br>a. The patient has a modified Medical Research Council [mMRC] dyspnea scale score of 2 or greater, **OR**<br>b. The patient has a COPD Assessment Test [CAT] score of 10 or greater **AND**<br>6. Must be experiencing dyspnea symptoms (persistent breathlessness or exercise limitation) despite treatment with a long-acting muscarinic antagonist and a long-acting beta-2 adrenergic agonist (LAMA + LABA) combination for at least 12 weeks **AND**<br>7. Must continue concomitant use of dual or triple therapy with Ohtuvayre<br>8. Ohtuvayre will not be authorized for any non-FDA approved diagnosis (e.g., asthma)<br>9. Ohtuvayre will not be authorized for use in combination with roflumilast<br>10. Initial approval will be for 6 months. Reauthorization for 12 months at a time will require documentation of the following:<br>a. Patient has experienced a decrease in symptoms while on therapy **AND**<br>b. Patient is continuing to use concomitant dual or triple maintenance therapy<br>11. Approved Dosage: See Ohtuvayre Prescribing Information<br>12. Quantity Limit: 60 ampules (150 mL)/30 days |

**POLICY GUIDELINES:**

1. Utilization Management are contract dependent and coverage criteria may be dependent on the contract renewal date. Additionally, coverage of drugs listed in this policy are contract dependent. Refer to specific contract/benefit language for exclusions.
2. Clinical documentation must be submitted for each request (initial and recertification) unless otherwise specified (e.g., provider attestation required). Supporting documentation includes, but is not limited to, progress notes documenting previous treatments/treatment history, diagnostic testing, laboratory test results, genetic testing/biomarker results, imaging and other objective or subjective measures of benefit which support continued use of the requested product is medically necessary. Also, ongoing use of the requested product must continue to reflect the current policy's preferred formulary. Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e., generics, biosimilars, or other guideline supported treatment options). Requested dosing must continue to be consistent with FDA-approved or off-label/guideline-supported dosing recommendations.
    - Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition.
3. Supportive documentation of previous drug use must be submitted for any criteria that require a trial of a preferred agent if the preferred drug is not found in claims history.
4. This policy does not apply to Medicare Part D and D-SNP pharmacy benefits. The drugs in this policy may apply to all other lines of business including Medicare Advantage.
5. For members with Medicare Advantage, medications with a National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) will be covered pursuant to the criteria outlined by the NCD and/or LCD. NCDs/LCDs for applicable medications can be found on the CMS website at https://www.cms.gov/medicare-coverage-database/search.aspx. Indications that have not been addressed by the applicable medication's LCD/NCD will be covered in accordance with criteria determined by the Health Plan (which may include review per the Health Plan's Off-Label Use of FDA Approved Drugs policy). Step therapy requirements may be imposed in addition to LCD/NCD requirements.
6. Not all contracts cover all Medical Infusible drugs. Refer to specific contract/benefit plan language for exclusions of Injectable Medications.
7. For contracts where Insurance Law § 4903(c-1), and Public Health Law § 4903(3-a) are applicable, if trial of preferred drug(s) is the only criterion that is not met for a given condition, and one of the following circumstances can be substantiated by the requesting provider, then trial of the preferred drug(s) will not be required.
    - The required prescription drug(s) is (are) contraindicated or will likely cause an adverse reaction or physical or mental harm to the member;
    - The required prescription drug is expected to be ineffective based on the known clinical history and conditions and concurrent drug regimen;
    - The required prescription drug(s) was (were) previously tried while under the current or a previous health plan, or another prescription drug or drugs in the same pharmacologic class or with the same mechanism of action was (were) previously tried and such prescription drug(s) was (were) discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event;
    - The required prescription drug(s) is (are) not in the patient’s best interest because it will likely cause a significant barrier to adherence to or compliance with the plan of care, will likely worsen a comorbid condition, or will likely decrease the ability to achieve or maintain reasonable functional ability in performing daily activities;

- The individual is stable on the requested prescription drug. The medical profile of the individual (age, disease state, comorbidities), along with the rational for deeming stability as it relates to standard medical practice and evidence-based practice protocols for the disease state will be taken into consideration.
- The above criteria are not applicable to requests for brand name medications that have an AB rated generic. We can require a trial of an AB-rated generic equivalent prior to providing coverage for the equivalent brand name prescription drug.

8. This policy is applicable to drugs that are included on a specific drug formulary (Rx benefit only). If a drug referenced in this policy is non-formulary, please reference the Non-formulary Medication Exception Review Policy for review guidelines.
9. Dose and frequency should be in accordance with the FDA label or recognized compendia (for off-label uses). When services are performed in excess of established parameters, they may be subject to review for medical necessity.
10. All requests will be reviewed to ensure they are being used for an appropriate indication and may be subject to an off-label review in accordance with our Off-Label Use of FDA Approved Drugs Policy (Pharmacy-32).
11. All utilization management requirements outlined in this policy are compliant with applicable New York State insurance laws and regulations. Policies will be reviewed and updated as necessary to ensure ongoing compliance with all state and federally mandated coverage requirements.
12. Manufacturers may either discontinue participation in, or may not participate in, the Medicaid Drug Rebate Program (MDRP). Under New York State Medicaid requirements, physician-administered drugs must be produced by manufacturers that participate in the MDRP. Products made by manufacturers that do not participate in the MDRP will not be covered under Medicaid Managed Care/HARP lines of business. Drug coverage will not be available for any product from a non-participating manufacturer. For a complete list of New/Reinstated & Terminated Labelers please visit: https://www.medicaid.gov/medicaid/prescriptiondrugs/medicaid-drug-rebate-program/newreinstated-terminated-labeler-information/index.html

**CODES:**

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.

CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

Code Key:
Experimental/Investigational = (E/I),
Not medically necessary/ appropriate = (NMN).


**HCPCS**:

J7601 Ohtuvayre

## UPDATES:

| Date | Revision |
|---|---|
| **02/12/2026** | P&T Committee Approval |
| 11/19/2025 | Revised |
| 03/07/2025 | Revised |
| 03/06/2025 | Revised |
| 02/07/2025 | Revised; P&T Committee reviewed and approved criteria changes on 02/06/2025 |
| 01/24/2025 | Created and Implemented |
| 11/21/2024 | P&T Committee Approval |

## REFERENCES:

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD); Global Strategy for Prevention, Diagnosis, and Management of COPD: 2025 Report. Available at https://goldcopd.org/2025-gold-report. Accessed December 26th, 2024.
2. Yang IA, Jenkins CR, Salvi SS. Chronic obstructive pulmonary disease in never-smokers: risk factors, pathogenesis, and implications for prevention and treatment. Lancet Respir Med. 2022 May;10(5):497-511. doi: 10.1016/S2213-2600(21)00506-3. Epub 2022 Apr 12. PMID: 35427530.
3. Ohtuvayre™ (ensifentrine) inhalation suspension [prescribing information]. Raleigh, NC: Verona Pharma, Inc.; revised 6/2024.
4. Anzueto A, Barjaktatrevic IZ, Siler TM, et al. Ensifentrine, a Novel Phosphodiesterase 3 and 4 Inhibitor for the Treatment of Chronic Obstructive Pulmonary Disease: Randomized, Double-Blind, Placebo-controlled, Multicenter Phase III Trials (the ENHANCE trials). Am J Respir Crit Care Med 2023; 208(4): 406-16.