MEDICAL MUTUAL®

Drug Policy

Policy:	Ohtuvayre (ensifentrine inhalation suspension, for oral inhalation use)	Annual Review Date: 03/20/2025 Last Revised Date: 03/20/2025

OVERVIEW

Ohtuvayre (ensifentrine) is indicated for the maintenance of chronic obstructive pulmonary disease (COPD) in adult patients. It is the first dual phosphodiesterase 3 (PDE3) and phosphodiesterase 4 (PDE4) inhibitor to be approved. It works through both bronchodilator and anti-inflammatory effects.

POLICY STATEMENT

This policy involves the use of Ohtuvayre. Prior authorization is recommended for pharmacy benefit coverage of Ohtuvayre. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Ohtuvayre as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Ohtuvayre be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Ohtuvayre is recommended in those who meet the following criteria:

1. **Chronic Obstructive Pulmonary Disease (COPD); Initial Therapy**
   Criteria. *Patient must meet the following criteria (A, B, C, D, E, F, and G)*
   - A. The patients is ≥18 years of age; AND
   - B. The patient has symptomatic disease demonstrated by Modified Medical Research Council (mMRC) score ≥2 or COPD Assessment Test (CAT) score ≥10; AND
   - C. The patient has a diagnosis of COPD confirmed with spirometry ([FEV1/FVC] ratio <0.7)*; AND
   - D. Individual has moderate to severe airflow obstruction demonstrated by post-bronchodilator FEV1 30-70% predicted normal*; AND
   - E. The patient has tried and experienced inadequate efficacy OR significant intolerance with a long-acting muscarinic antagonist (LAMA) product; AND

Note: Products containing a LAMA include Incruse Ellipta, tiotropium inhaler (Spiriva HandiHaler, generics), Spiriva Respimat, Tudorza Pressair, and LAMA/LABA inhalers Anoro Ellipta, Bevespi Aerosphere, Duaklir Pressair, Stiolto Respimat.

F. The patient has tried and experienced inadequate efficacy OR significant intolerance with a long-acting beta-agonist (LABA) product; AND
Note: Products containing a LABA include Serevent Diskus, Striverdi Respimat, formoterol fumarate inhalation solution (Perforomist, generics), and LAMA/LABA inhalers Anoro Ellipta, Bevespi Aerosphere, Duaklir Pressair, Stiolto Respimat, and ICS/LABA Inhalers fluticasone-salmeterol HFA (Advair HFA, authorized generic), fluticasone-salmeterol diskus, Wixela (Advair Diskus, generics), fluticasone-vilanterol (Breo Ellipta, authorized generic), Dulera, fluticasone-salmeterol respiclock (AirDuo RespiClick, authorized generic), AirDuo Digihaler, or budesonide-formoterol (Symbicort, generics).
G. The medication is prescribed by or in conjunction with pulmonary specialist.

2. Chronic Obstructive Pulmonary Disease (COPD); Continuation of Therapy
Criteria. *Patient must meet the following criteria (A, B, C, D, E, and F):*

A. The patients is ≥ 18 years of age; AND
B. The patient has a diagnosis of COPD confirmed with spirometry ([FEV1/FVC] ratio <0.7); AND
C. The patient has tried and experienced inadequate efficacy OR significant intolerance with a long-acting muscarinic antagonist (LAMA) product; AND
Note: Products containing a LAMA include Incruse Ellipta, tiotropium inhaler (Spiriva HandiHaler, generics), Spiriva Respimat, Tudorza Pressair, and LAMA/LABA inhalers Anoro Ellipta, Bevespi Aerosphere, Duaklir Pressair, Stiolto Respimat.
D. The patient has tried and experienced inadequate efficacy OR significant intolerance with a long-acting beta-agonist (LABA) product; AND
Note: Products containing a LABA include Serevent Diskus, Striverdi Respimat, formoterol fumarate inhalation solution (Perforomist, generics), and LAMA/LABA inhalers Anoro Ellipta, Bevespi Aerosphere, Duaklir Pressair, Stiolto Respimat, and ICS/LABA Inhalers fluticasone-salmeterol HFA (Advair HFA, authorized generic), fluticasone-salmeterol diskus, Wixela (Advair Diskus, generics), fluticasone-vilanterol (Breo Ellipta, authorized generic), Dulera, fluticasone-salmeterol respiclock (AirDuo RespiClick, authorized generic), AirDuo Digihaler, or budesonide-formoterol (Symbicort, generics).
E. The medication is prescribed by or in conjunction with pulmonary specialist; AND
F. The patient has had a response to therapy including reduced symptoms, reduced frequency of exacerbations, or reduced severity of exacerbations.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 6 months
B) *Extended Approval:* 1 year

CONDITIONS NOT RECOMMENDED FOR APPROVAL

MEDICAL MUTUAL®

Drug Policy

Ohtuvayre has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Asthma.** Ohtuvayre is not indicated for the use of Asthma.
2. **Bronchiectasis.** Ohtuvayre is not indicated for the use of bronchiectasis.
3. **Cystic fibrosis.** Ohtuvayre is not indicated for the use of cystic fibrosis.
4. **Concurrent use with roflumilast.** Duplicate therapy with another phosphodiesterase-4 (PDE4) inhibitor is not recommended.
5. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

***Documentation Requirements:**
The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational, or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Ohtuvayre™ inhalation suspension [prescribing information]. Raleigh, NC: Verona Pharma, Inc.; June 2024.
2. Anzueto A, 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):406416.
3. Han MLK, et al. Chronic obstructive pulmonary disease: Diagnosis and staging. Stoller JK, Dieffenbach P, eds. UpToDate. Waltham, MA: UpToDate Inc. Updated June 5, 2024. Accessed August 6, 2024.
4. Liu Y, et al. Trends in the prevalence of chronic obstructive pulmonary disease among adults aged ≥18 years – United States, 2011-2021. MMWR Morb Mortal Wkly Rep. 2023;72(46):12501256.