Example Letter of Appeal

The example letter on page 2 regarding appeals is for demonstration purposes only. Any language, section, or clinical detail may be added, removed, or modified as necessary to accurately reflect the patient's clinical circumstances and the prescriber's medical judgment. Use of this example letter or the information in this example letter does not guarantee coverage. It is not intended to be a substitute for, or to influence, the independent clinical decision of the prescribing healthcare professional.

Ohtuvayre® (ensifentrine) Inhalation Suspension 3 mg/2.5 mL

INDICATION

OHTUVAYRE® (ensifentrine) is indicated for the maintenance treatment of chronic obstructive pulmonary disease (COPD) in adult patients.

SELECTED SAFETY INFORMATION

Contraindications: OHTUVAYRE is contraindicated in patients with hypersensitivity to ensifentrine or any component of this product.

Warnings and Precautions:

Acute Episodes of Bronchospasm: OHTUVAYRE should not be used for the relief of acute symptoms, i.e., as rescue therapy for the treatment of acute episodes of bronchospasm. OHTUVAYRE has not been studied in the relief of acute symptoms and extra doses of OHTUVAYRE should not be used for that purpose. Acute symptoms should be treated with an inhaled, short-acting bronchodilator.

Paradoxical Bronchospasm: As with other inhaled medicines, OHTUVAYRE may produce paradoxical bronchospasm, which may be life threatening. If paradoxical bronchospasm occurs following dosing with OHTUVAYRE, it should be treated immediately with an inhaled, short-acting bronchodilator. OHTUVAYRE should be discontinued immediately and alternative therapy should be instituted.

Psychiatric Events Including Suicidality: Treatment with OHTUVAYRE is associated with an increase in psychiatric adverse reactions. Psychiatric events including suicide-related adverse reactions were reported in clinical studies in patients who received OHTUVAYRE (1 suicide attempt and 1 suicide). Additionally, the most commonly reported psychiatric adverse reactions in the pooled 24-week safety population were insomnia (6 patients [0.6%] OHTUVAYRE 3 mg; 2 patients [0.3%] placebo), and anxiety (2 patients [0.2%] OHTUVAYRE 3 mg; 1 patient [0.2%] placebo). Depression-related reactions including depression, major depression, and adjustment disorder with depressed mood occurred in 4 patients (0.4%) receiving OHTUVAYRE and no patients receiving placebo.

Before initiating treatment with OHTUVAYRE, healthcare providers should carefully weigh the risk and benefits of treatment with OHTUVAYRE in patients with a history of depression and/or suicidal thoughts or behavior. Patients, their caregivers, and families should be advised of the need to be alert for the emergence or worsening of insomnia, anxiety, depression, suicidal thoughts, or other mood changes, and if such changes occur to contact their healthcare provider. Healthcare providers should carefully evaluate the risks and benefits of continuing treatment with OHTUVAYRE if such events occur.

Adverse Reactions: The most common adverse reactions ≥1% in OHTUVAYRE and greater than placebo in the pooled population were back pain 1.8%, hypertension 1.7%, urinary tract infection 1.3%, and diarrhea 1.0%.

These are not all of the possible risks associated with OHTUVAYRE.

SPECIAL POPULATIONS

Pediatric Use: The safety and effectiveness of OHTUVAYRE have not been established in pediatric patients.

Lactation: There are no data on the presence of ensifentrine in human milk, the effects on the breastfed child, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for OHTUVAYRE and any potential adverse effects on the breastfed child from OHTUVAYRE or from the underlying maternal condition.

Geriatric Use: In clinical trials, patients aged 65 and older showed no overall differences in the safety or effectiveness of OHTUVAYRE compared with younger adults, but greater sensitivity in some older individuals cannot be ruled out.

Hepatic Impairment: Ensifentrine systemic exposure increased by 2.3-fold in subjects with moderate or severe hepatic impairment compared with healthy subjects. Use OHTUVAYRE with caution in patients with hepatic impairment.

Before prescribing OHTUVAYRE, please read the accompanying Prescribing Information. The Patient Information is also available.

Continue to page 2 for an Example Letter of Appeal that can be completed and submitted to the payer.

MERCK

<Date>
ATTENTION: <Medical Director Name and/or Medical Review/Appeals>
<Payer/Health Plan Name>
<Payer Address>

REGARDING: <Appeal Letter or Prior Authorization Denial> for OHTUVAYRE® (ensifentrine) for oral inhalation 3 mg/2.5 mL

PATIENT NAME: <Patient Name>
DATE OF BIRTH: <Patient Date of Birth>
POLICY ID NUMBER: <Policy ID Number>
PROVIDER ID NUMBER:

MEMBER NAME: <Member Name>
MEMBER NUMBER: <Member Number>
GROUP NUMBER: <Group Number>
DIAGNOSIS: <ICD-10 code>
PATIENT DOSAGE: <Patient Dosage>

☐ **STANDARD** ☐ **URGENT**

Dear <Medical Director Name and/or Medical Review/Appeals>,

I am writing to request reconsideration of coverage for OHTUVAYRE for my patient, <Patient Name>, who has been diagnosed with chronic obstructive pulmonary disease (COPD). <Payer Name> has denied coverage of OHTUVAYRE due to <OHTUVAYRE is not on formulary or reason for PA denial, as indicated on the Denial Letter>.

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. I believe that therapy with OHTUVAYRE is appropriate for this patient. Attached to this request are clinical notes regarding this patient's disease state, the OHTUVAYRE package insert, and relevant medical records, test results, and publications, including clinical trials and treatment guidelines or expert recommendations.

<In this rationale for treatment, you may wish to include the following:

[Commercial/Medicare Advantage/Medicaid/Medicare Fee-for-Service]
- Summary of patient's COPD diagnosis, including:
  - Diagnosis (ICD-10-CM) and date of diagnosis
  - Relevant test results and clinical measures, which may include:
    - Spirometry parameters such as pre- and post-bronchodilator forced expiratory volume (FEV1)/forced vital capacity (FVC) ratio and post-bronchodilator FEV1 % predicted
    - Vital signs (eg, respiratory rate, heart rate)
    - Oxygenation status (eg, oxygen saturation)
  - Patient's current clinical condition (eg, symptoms and disease severity)
    - Modified Medical Research Council (mMRC) dyspnea scale grade ≥ 2
    - COPD Assessment Test (CAT) score ≥ 10
  - Patient's functional status/ability to use inhalation devices
  - Patient's clinical history (eg, history of chronic bronchitis, dyspnea during everyday activities, COPD-related dyspnea despite dual or triple maintenance therapy as indicated by persistent breathlessness or exercise limitation, hospitalization/emergency room visit due to COPD exacerbation)
- Any relevant COPD therapies the patient is currently using or has previously used, including intolerance to another drug class, such as an oral PDE4 inhibitor, LAMA, LABA, ICS
- Assessment of symptom burden using a validated patient-reported tool (eg, Dyspnea Visual Analog Scale [VAS])
- Provide your professional opinion on potential implications for your patient's condition if they do not receive treatment with OHTUVAYRE
- Consider including your medical credentials for treating patients with COPD>

(Continues on next page)

Thank you for taking the time to read this letter. For the reasons above, and based on my medical opinion, I believe that treatment with OHTUVAYRE is appropriate for this patient. I look forward to your prompt review of this request. My office may be reached at <office phone number> or <email address> if any additional information is required.

Best regards,

<Physician Name>

<FEV1, forced expiratory volume; FVC, forced vital capacity; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; ICS, inhaled corticosteroid; LABA, long-acting beta-agonist; LAMA, long-acting muscarinic antagonist.>

Enclosures:

<Suggested enclosures include:
• Clinical notes regarding this patient's disease state
• OHTUVAYRE package insert
• Relevant medical records and test results
• Relevant publications, including clinical trials and treatment guidelines>