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

For the maintenance treatment of COPD

A novel approach to bronchodilation and non-steroidal anti-inflammation[1-9]

Indication and Important Safety Information

INDICATION

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

IMPORTANT SAFETY INFORMATION

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

Please see Full Important Safety Information throughout and Full Prescribing Information also available at OhtuvayreHCP.com.

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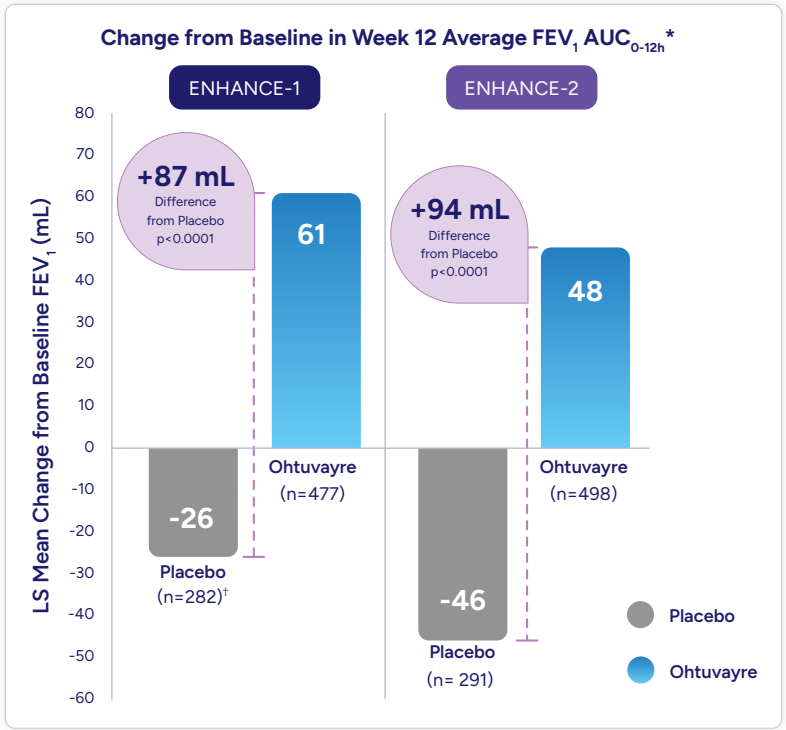
Significant improvement in lung function[1,2]



Ohtuvayre was studied in two 24-week, randomized, double-blind, placebo-controlled studies in patients with symptomatic, moderate to severe COPD (N=1553). Patients were allowed to continue their background maintenance medication regimen (i.e., LAMA or LABA, with or without ICS or no background medication).[1,2]

Primary endpoint: change from baseline in FEV_1 AUC_{0-12h} at Week 12.[1]

*Average FEV_1 AUC_{0-12h} is defined as the AUC over 12 hours of the FEV_1, divided by 12 hours.[2]
†One patient was randomized to placebo and treated but was not included in the endpoint analysis due to missing baseline FEV_1.[10]

AUC = area under the curve; FEV_1 = forced expiratory volume in one second; ICS = inhaled corticosteroids; LABA = long-acting beta-agonist; LAMA = long-acting muscarinic antagonist; LS = least-squares.

Appropriate for a broad patient population, including those who are symptomatic on maintenance therapy.[1,2]

- **62%** of patients were on a long-acting bronchodilator treatment[2]
  - **18%** were also on an inhaled corticosteroid[2]
- **38%** had no concomitant maintenance COPD therapy[2]

Incidence rates were low and similar to placebo[1,2]

Pooled ENHANCE Adverse Reactions*

	Ohtuvayre N= 975	Placebo N=574
Back Pain	1.8%	1.0%
Hypertension	1.7%	0.9%
Urinary Tract Infection	1.3%	1.0%
Diarrhea	1.0%	0.7%

Adverse reactions ≥1% and more common than placebo.[1]

*Pooled 24-week ENHANCE-1 and ENHANCE-2 safety population.[1]

Discontinuation rate due to adverse reactions was low and similar to placebo.

- 7.6% in the Ohtuvayre group vs 8.2% on placebo[1]

Adverse reactions in the 48-week cohort were consistent with those observed in the pooled 24-week safety population.[1]

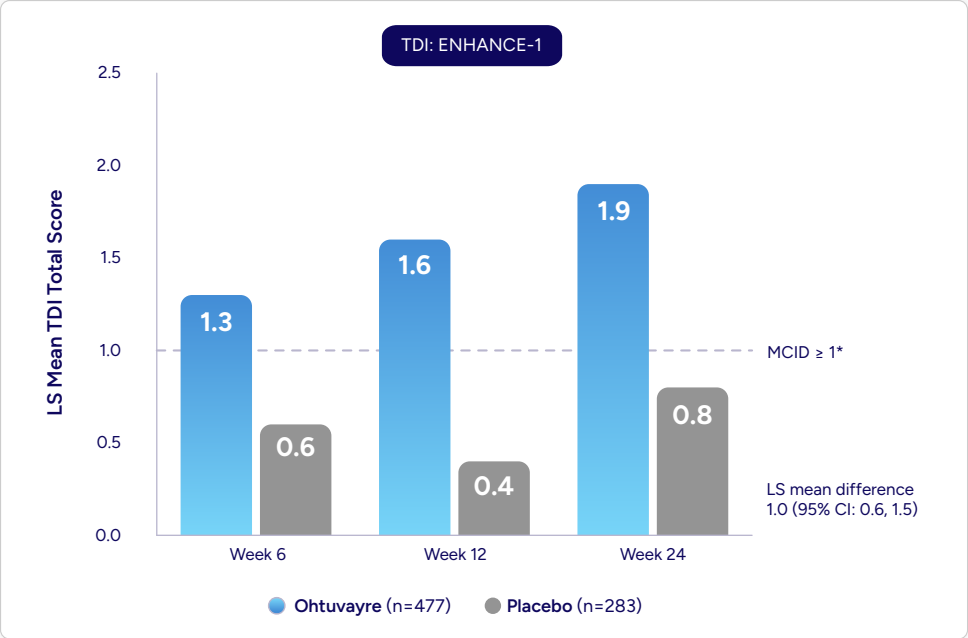
IMPORTANT SAFETY INFORMATION (cont'd)

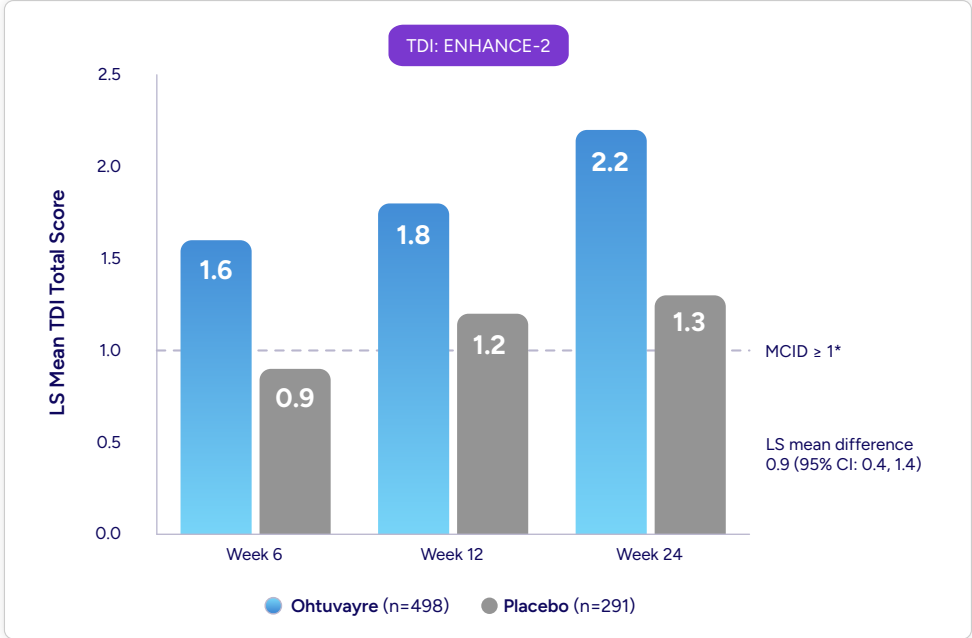
Warnings and Precautions:

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. Acute symptoms should be treated with an inhaled, short-acting bronchodilator.

Please see Full Important Safety Information throughout and Full Prescribing Information also available at OhtuvayreHCP.com.

Transition Dyspnea Index (TDI) scores over 24 weeks[2,10]





TDI was evaluated for Ohtuvayre compared with placebo in ENHANCE-1 and ENHANCE-2 as prespecified secondary endpoints.[2,10]

These observations are descriptive only, as they are not included in the statistical hierarchy and therefore not controlled for multiplicity.[2,10]

IMPORTANT SAFETY INFORMATION (cont'd)

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.

*Minimal clinically important difference (MCID) for TDI is 1 unit.[2]
LS = least-squares.

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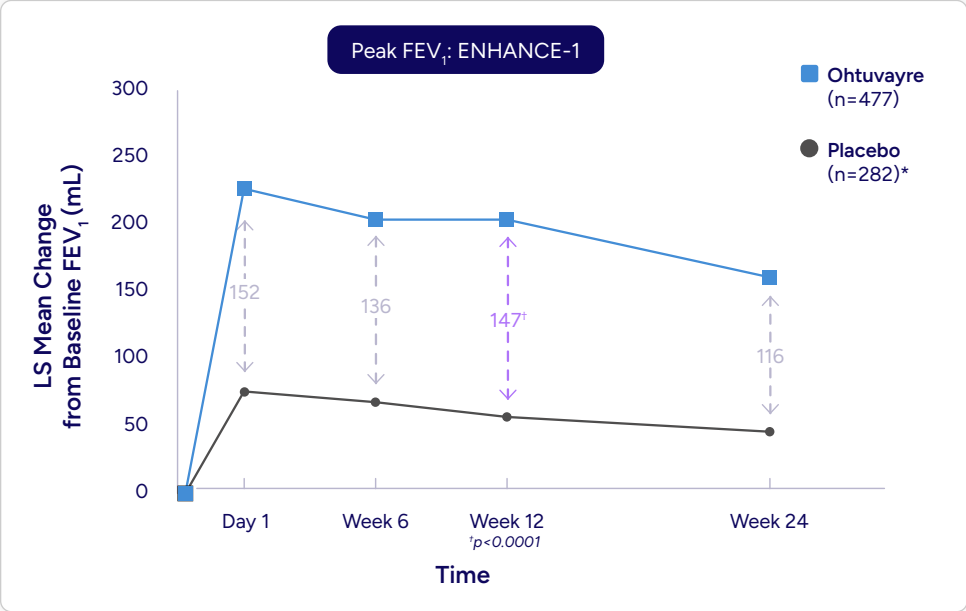
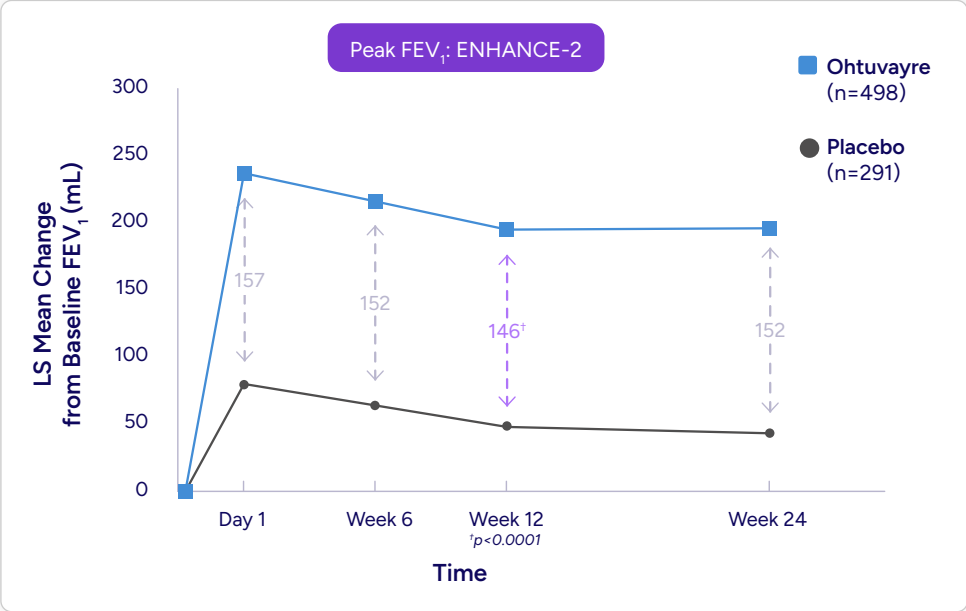
Better breathing as early as Day 1[2,10]





Key secondary endpoint: Peak FEV_1 evaluated at Week 12 was included in the statistical testing hierarchy. Peak FEV_1 at other timepoints were not included in the statistical hierarchy for ENHANCE-1 and ENHANCE-2 and therefore not controlled for multiplicity.[2,10]

Peak FEV_1 was defined as the highest post-dose FEV_1 within the first 4 hours after dosing.[2]

*One patient was randomized to placebo and treated but was not included in the endpoint analysis due to missing baseline FEV_1.[10]

FEV_1 = forced expiratory volume in one second; LS = least-squares.

IMPORTANT SAFETY INFORMATION (cont'd)

Psychiatric Events Including Suicidality 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.

IMPORTANT SAFETY INFORMATION (cont'd)

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.

Please see Full Important Safety Information throughout and Full Prescribing Information also available at OhtuvayreHCP.com.

Prescribe through Verona Pathway Plus™

Pathway Plus is a support program that offers help and resources to you and your patients throughout treatment.

- Insurance coverage verification
- Specialty pharmacy network coordination
- Access support from our field reimbursement managers
- Patient welcome kit and call from our dedicated care coordinators
- Financial assistance options for eligible patients

Step 1

Complete the Prescription Form and the Patient Enrollment and Consent Form

- Patient consent is required for the patient to access affordability support programs from Verona Pathway Plus

Step 2

Fax the completed forms to Verona Pathway Plus at **833-392-8999**

- Alternatively, you may e-prescribe to PHYZ pharmacy (NCPDP 5828809)

Visit OhtuvayreHCP.com/access-patient-support/resources/ to download the Prescription and Enrollment forms and to learn more about how to e-prescribe.

Access and financial support

Copay Program

Eligible commercially insured patients may pay as little as $0 per month for Ohtuvayre.*

Patient Assistance Program

Provides financial assistance options for patients who do not have insurance or are underinsured.

- Patient Assistance Program Prescription required

Ohtuvayre Bridge Program

Available to eligible patients during a coverage delay.

- Bridge Program Prescription required

*Terms, conditions, and program maximums apply. This program is not open to patients receiving prescription reimbursement under any federal, state, or government-funded healthcare program. Not valid where prohibited by law.

Not actual patient

If your patient cannot afford their medication, have them contact Verona Pathway Plus at 1-833-372-8492. We may be able to help.

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See what Ohtuvayre could mean for your patients at OhtuvayreHCP.com.

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Recommended in the 2025 GOLD Report

The GOLD Report now includes Ohtuvayre in the follow-up treatment algorithm for patients experiencing persistent dyspnea, acknowledging the following benefits[11]:

- A novel first-in-class inhaled dual inhibitor of PDE3 and PDE4, combining anti-inflammatory activity with bronchodilator effects

GOLD = Global Initiative for Chronic Obstructive Lung Disease; PDE = phosphodiesterase.

IMPORTANT SAFETY INFORMATION (cont'd)

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. **Please see the Full Prescribing Information for Ohtuvayre.**

To report suspected adverse reactions, contact Verona Pharma, Inc. at 1-888-672-0371 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Got questions?
Reach out to your rep today!

Need a Rep?
Request a Rep to get further information about prescribing, insurance, coverage, efficacy, and safety of Ohtuvayre.

References:
1. Ohtuvayre™ (ensifentrine). Prescribing Information. Raleigh, NC: Verona Pharma plc; 2024. **2.** Anzueto A, Barjaktarevic 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):406-416. **3.** Cazzola M, Hanania NA, Page CP, Matera MG. Novel anti-inflammatory approaches to COPD. *Int J Chron Obstruct Pulmon Dis.* 2023;18:1333-1352. **4.** Singh D, Abbott-Banner K, Bengtsson T, Newman K. The short-term bronchodilator effects of the dual phosphodiesterase 3 and 4 inhibitor RPL554 in COPD. *Eur Respir J.* 2018;52:1801074. **5.** Singh D, Martinez FJ, Watz H, Bengtsson T, Maurer BT. A dose-ranging study of the inhaled dual phosphodiesterase 3 and 4 inhibitor ensifentrine in COPD. *Respir Res.* 2020;21:47. **6.** Ferguson GT, Kerwin EM, Rheault T, Bengtsson T, Rickard K. A dose-ranging study of the novel inhaled dual PDE 3 and 4 inhibitor ensifentrine in patients with COPD receiving maintenance tiotropium therapy. *Int J Chron Obstruct Pulmon Dis.* 2021;16:1137-1148. **7.** Boswell-Smith V, Spina D, Oxford AW, Comer MB, Seeds EA, Page CP. The pharmacology of two novel long-acting phosphodiesterase 3/4 inhibitors, RPL554 [9,10-dimethoxy-2(2,4,6-trimethylphenylimino)-3-(N-carbamoyl-2-aminoethyl)-3,4,6,7-tetrahydro-2H-pyrimido[6,1-a]isoquinolin-4-one] and RPL565 [6,7-dihydro-2-(2,6-diisopropylphenoxy)-9,10-dimethoxy-4H-pyrimido[6,1-a]isoquinolin-4-one]. *J Pharmacol Exp Ther.* 2006;318(2):840-848. **8.** Rheault T, MacDonald-Berko M. Anti-inflammatory pharmacology of ensifentrine. Poster presented virtually at: CHEST Annual Meeting; October 18-21, 2020. **9.** Franciosi LG, Diamant Z, Banner KH, et al. Efficacy and safety of RPL554, a dual PDE3 and PDE4 inhibitor, in healthy volunteers and in patients with asthma or chronic obstructive pulmonary disease: findings from four clinical trials. *Lancet Respir Med.* 2013;1(9):714-727. **10.** Data on File. Verona Pharma plc: Raleigh, NC. **11.** Global Initiative for Chronic Obstructive Lung Disease. *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. (2025 Report).* Global Initiative for Chronic Obstructive Lung Disease; 2024.

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