Trelegy Ellipta (fluticasone furoate, umeclidinium, vilanterol)

FIRST LOOK: NEW INDICATION

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Trelegy Ellipta

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Introduction

- **Brand name:** Trelegy Ellipta
- **Generic name:** Fluticasone furoate, umeclidinium, vilanterol
- **Pharmacologic class:** Corticosteroid + anticholinergic + long-acting beta$_2$-adrenergic agonist (LABA)
- **Strength and Formulation:** 100/62.5/25mcg; 200/62.5/25mcg; per inhalation; dry powder for oral inhalation
- **Manufacturer:** GlaxoSmithKline
- **How supplied:** Dry powder inhaler—30 doses
- **Legal Classification:** Rx

New Indication

- Maintenance treatment of **asthma** in patients aged 18 years and older.
  - *Limitation of use*: Not indicated for relief of acute bronchospasm.

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Other Indication(s)

- **Trelegy Ellipta 100/62.5/25mcg** is also indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).

Mechanism of Action

- **Fluticasone furoate** is a synthetic trifluorinated corticosteroid with anti-inflammatory activity.
- **Umeclidinium** is a long-acting muscarinic antagonist (anticholinergic) that causes bronchodilation through M3 receptor inhibition at the smooth muscle.
- **Vilanterol** is a LABA that relaxes smooth muscle and inhibits release of mediators of immediate hypersensitivity from cells.

Dosage & Administration: Asthma

- 1 inhalation of **100/62.5/25mcg** or **200/62.5/25mcg** once daily.
- Maximum: 1 inhalation of **200/62.5/25mcg** once daily.
- Rinse mouth after use.
- Consider other therapeutic regimens and additional therapeutic options if patient does not respond adequately to 200/62.5/25mcg.

- *See full labeling for additional dosing information.*

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Clinical Trial: Asthma

- Approval was based on a randomized, double-blind, active-controlled, parallel group confirmatory trial (NCT02924688) that evaluated the efficacy and safety of Trelegy Ellipta in 2436 adult patients with asthma inadequately controlled on their current treatments of combination therapy (inhaled corticosteroid [ICS] plus a LABA).
- Patients with an Asthma Control Questionnaire (ACQ-6) score ≥1.5 on current treatment of ICS plus LABA entered a 3-week run-in period with fluticasone propionate/salmeterol 250/50mcg twice daily.
- After the 3-week run-in period, patients who remained inadequately controlled (ACQ-6 ≥1.5) were transferred to fluticasone furoate/vilanterol 100/25mcg once daily for a 2-week stabilization period.

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Clinical Trial: Asthma

- After the 5-week run-in/stabilization period, eligible patients were randomized to receive 1 of the following treatments once daily:
  - Trelegy Ellipta 100/62.5/25mcg (n=406)
  - Trelegy Ellipta 200/62.5/25mcg (n=408)
  - Fluticasone furoate/umeclidinium/vilanterol 100/31.25/25mcg (n=405)
  - Fluticasone furoate/umeclidinium/vilanterol 200/31.25/25mcg (n=404),
  - Fluticasone furoate/vilanterol (FF/VI) 100/25mcg (n=407)
  - FF/VI 200/25mcg (n=406)

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Clinical Trial: Asthma

- **Patient demographics**
  - Mean age: 53 years; 80% White; 62% female; 81% never smoked.
  - Mean asthma duration: 21 years (range 1 to 70).
- The **trial excluded** current smokers and past smokers with an average smoking history of 4.3 pack-years.
- In the prior 12 months:
  - 85% reported having exacerbations.
  - ~63% reported having exacerbations that required oral/systemic corticosteroids and/or hospitalization.

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Clinical Trial: Asthma

- **At screening**
  - Mean prebronchodilator percent predicted forced expiratory volume in 1 second (FEV_1) was 58.5%.
  - Mean percent reversibility was 29.9%.
  - Mean absolute reversibility: 484mL
  - Mean ACQ-6 score: 2.5
- **During the 5-week run-in/stabilization period**
  - Trough FEV_1 improvement of 287mL.
  - Mean ACQ-6 score decreased by 0.6.
- **At randomization**
  - Majority (93%) remained not well controlled (mean ACQ-6 score of 1.9)
  - Mean prebronchodilator percent predicted FEV_1 was 68.2%

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Clinical Trial: Asthma

- The **primary end point** was the change from baseline in trough forced expiratory volume in 1 second (FEV_1) at 24 weeks.

Clinical Trial: Asthma

- Least squares **mean change from baseline in trough FEV_1** at week 24:
  - Trelegy Ellipta 100/62.5/25mcg vs FF/VI 100/25mcg difference: 110mL (95% CI, 66-153mL; *P* <.001).
  - Trelegy Ellipta 200/62.5/25mcg vs FF/VI 200/25mcg difference: 92mL (95% CI, 49-135mL; *P* <.001).
- Change from baseline in FEV_1 at **3 hours post-dose** was supportive of the primary end point with improvements for Trelegy Ellipta:
  - Trelegy Ellipta 100/62.5/25mcg vs FF/VI 100/25mcg (111mL, 95% CI, 67-155mL).
  - Trelegy Ellipta 200/62.5/25mcg vs FF/VI 200/25mcg (118mL, 95% CI, 74-162mL).

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Clinical Trial: Asthma

- Mean annualized rate of **asthma exacerbations:**
  - Pooled analysis: 0.31 for Trelegy Ellipta vs 0.31 for FF/VI.
  - Unpooled analysis: 0.41 for Trelegy Ellipta 100/62.5/25mcg and 0.23 for Trelegy Ellipta 200/62.5/25mcg vs 0.38 for FF/VI 100/25mcg and 0.26 for FF/VI 200/25mcg.
- **Asthma Control Questionnaire** (ACQ)-7 responder rate at week 24:
  - Pooled analysis: 63% for Trelegy Ellipta vs 55% for FF/VI
  - Unpooled analysis: 62% for Trelegy Ellipta 100/62.5/25mcg vs 52% for FF/VI 100/25mcg (OR 1.59; 95% CI, 1.18-2.13); 64% for Trelegy Ellipta 200/62.5/25mcg vs 58% for FF/VI 200/25mcg (OR 1.28; 95% CI, 0.95-1.72).

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Considerations for Specific Populations

- **Pregnancy:** Insufficient data to inform a drug-associated risk.
  - *Clinical Considerations*: Increased risk of perinatal outcomes in women with poorly or moderately controlled asthma.
  - *Labor or Delivery*: Use during late gestation and labor only if potential benefit justifies the risks.
- **Nursing mothers:** No available information; consider benefits of breastfeeding along with mother's clinical need for Trelegy Ellipta and any potential adverse effects.
- **Pediatric:** Not established in patients aged 17 years and younger.
- **Geriatric:** No dosage adjustment required.
- **Renal impairment:** Not studied.
- **Hepatic impairment:** Not studied.

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Contraindications

- Primary treatment of status asthmaticus or other acute episodes of COPD or asthma where intensive measures are required.
- Severe hypersensitivity to **milk proteins**.

Warnings and Precautions

- Use of LABA as monotherapy (without ICS) for asthma is associated with an increased risk of asthma-related death.
- Do not initiate in rapidly deteriorating or potentially life-threatening episodes of COPD or asthma.
- Not for use with other LABAs.
- Do not exceed recommended dose.
- Prescribe a short-acting, inhaled β_2-agonist for acute symptoms; monitor for increased need.

Warnings and Precautions

- Risk of oropharyngeal candidiasis: treat with appropriate local or systemic antifungal therapy if occurs.
- Monitor for signs/symptoms of pneumonia.
- Immunosuppression and risk of infections.
- Caution in patients with tuberculosis, systemic infections, or ocular herpes simplex.
- If exposed to chickenpox or measles, consider immune globulin or antiviral-prophylactic therapies.

Warnings and Precautions

- May unmask previously suppressed allergic conditions when transferring from systemic corticosteroid therapy to Trelegy Ellipta.
- Monitor for adrenal insufficiency when transferring from systemic steroids.
- Monitor for hypercorticism and HPA axis suppression (if occurs, discontinue gradually), intraocular pressure, glaucoma, or cataracts.
- Consider eye exams if ocular symptoms develop with long-term use.
- Reevaluate periodically.

Warnings and Precautions

- Discontinue if paradoxical bronchospasm occurs; use alternative therapy.
- Caution in patients with cardiovascular disease (esp. coronary insufficiency, arrhythmias, hypertension); consider discontinuing if significant effects occur.
- Assess bone mineral density prior to initiation and periodically thereafter if risk factors exist (eg, prolonged immobilization, osteoporosis, postmenopausal, advanced age, others).

Warnings and Precautions

- Caution in patients with urinary retention (esp. prostatic hyperplasia or bladder-neck obstruction).
- May produce significant hypokalemia or transient hyperglycemia.
- Use with caution in patients with convulsive disorders, thyrotoxicosis, diabetes mellitus and ketoacidosis.

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Interactions

- **Caution with**:
  - Concomitant strong CYP3A4 inhibitors (eg, ketoconazole, ritonavir, clarithromycin, conivaptan, indinavir, itraconazole, lopinavir, nefazodone, nelfinavir, saquinavir, telithromycin, troleandomycin, voriconazole).
  - K^+-depleting diuretics (eg, loop or thiazide diuretics).
- **Extreme caution with**:
  - MAOIs.
  - Tricyclic antidepressants.
  - Drugs known to prolong QTc interval or within 2 weeks of discontinuing such agents (increased risk of ventricular arrhythmias).

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Interactions

- Antagonized by β-blockers; if no acceptable alternatives, consider cardioselective agents.
- May be potentiated by anticholinergic drugs; avoid.

Adverse Reactions

- **COPD: Most common (≥1%)**
  - Upper respiratory tract infection (RTI), pneumonia, bronchitis, oral candidiasis, headache, back pain, arthralgia, influenza, sinusitis, pharyngitis, rhinitis, dysgeusia, constipation, urinary tract infection, diarrhea, gastroenteritis, oropharyngeal pain, cough, dysphonia.
- **Asthma: Most common (≥2%)**
  - Pharyngitis/nasopharyngitis, upper RTI/viral upper RTI, bronchitis, RTI/viral RTI, sinusitis/acute sinusitis, urinary tract infection, rhinitis, influenza, headache, back pain.
- **Other:** Hypersensitivity reactions.

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Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/trelegy-ellipta/