Trelegy Ellipta

(fluticasone furoate, umeclidinium, vilanterol)

NEW PRODUCT SLIDESHOW

MPR

Introduction

- **Brand name:** Trelegy Ellipta
- **Generic name:** Fluticasone furoate, umeclidinium, vilanterol
- **Pharmacological class:** Corticosteroid + anticholinergic + long-acting beta-2 agonist (LABA)
- **Strength and Formulation:** 100/62.5/25mcg; per inh; dry powder for oral inhalation
- **Manufacturer:** GlaxoSmithKline
- **How supplied:** Dry powder inhaler—30 doses
- **Legal Classification:** Rx

Trelegy Ellipta

Indications

- Long-term maintenance treatment of airflow obstruction in patients with **COPD**, including chronic bronchitis and/or emphysema
- To **reduce exacerbations** of COPD in patients with a history of exacerbations

Limitations of Use

- **Not indicated** for relief of acute bronchospasm or for treatment of asthma

Dosage & Administration

- 1 inhalation once daily (max)
- Rinse mouth after use

Considerations for Special Populations

- **Pediatric:** Not established
- **Pregnancy:** Insufficient human data to establish drug-associated risk
- **Nursing mothers:** Consider mother's need and potential adverse effects on child
- **Geriatric:** No dosage adjustment required
- **Renal impairment**: No dosage adjustment required
- **Hepatic impairment:** Studies on patients with severe impairment not performed

Contraindications

- Severe hypersensitivity to **milk proteins**

Warnings/Precautions

- Data from clinical trials in patients with COPD do not suggest an increased risk of death with LABA in COPD patients
  - LABA monotherapy (without ICS) for asthma is associated with increased risk of asthma-related death (Trelegy Ellipta is **not** indicated for asthma)
- Do not initiate in rapidly or acutely deteriorating COPD
- Not for use with other LABAs
- Do not exceed recommended dose
- Prescribe a short-acting, inhaled β2-agonist for acute symptoms; monitor for increased need
- Monitor for signs/symptoms of pneumonia

Warnings/Precautions

- Immunosuppressed
- Tuberculosis
- Systemic infections
- Ocular herpes simplex
- If exposed to chickenpox or measles, consider immune globulin or antiviral - prophylactic therapies
- Monitor for adrenal insufficiency when transferring from systemic steroids

Warnings/Precautions

- May need supplemental systemic corticosteroids during periods of stress or a severe COPD exacerbation
- May unmask previously suppressed allergic conditions
- Reevaluate periodically
- Monitor for hypercorticism and HPA axis suppression (if occurs, discontinue gradually), intraocular pressure, glaucoma, or cataracts

Warnings/Precautions

- **Discontinue** if paradoxical bronchospasm occurs; use alternative therapy
- Cardiovascular disease (esp. coronary insufficiency, arrhythmias, hypertension); discontinue if significant effects occur
- Convulsive disorders
- Thyrotoxicosis
- Hyperresponsiveness to sympathomimetics
- Diabetes
- Ketoacidosis

Warnings/Precautions

- Hypokalemia
- Hyperglycemia
- Urinary retention
- Prostatic hyperplasia
- Bladder-neck obstruction
- Assess bone mineral density if risk factors exist (eg, prolonged immobilization, osteoporosis, postmenopausal, advanced age, others)
- Labor & delivery

Interactions

- **Caution** with:
  - Concomitant strong CYP3A4 inhibitors (eg, ketoconazole, ritonavir, clarithromycin, conivaptan, indinavir, itraconazole, lopinavir, nefazodone, nelfinavir, saquinavir, telithromycin, troleandomycin, voriconazole)
  - MAOIs
  - Tricyclic antidepressants

Interactions

- **Caution** with:
  - Drugs known to prolong the QT interval or within 2 weeks of discontinuing such agents (increased cardiac effects)
  - K^+-depleting diuretics
- Antagonized by β-blockers; if needed, consider cardioselective agents
- Additive effects with concomitant other anticholinergic-containing drugs; avoid

Adverse Reactions

- Headache
- Back pain
- Dysgeusia
- Diarrhea
- Cough
- Oropharyngeal pain
- Gastroenteritis
- Oral candidiasis
- Hypersensitivity reactions

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

Clinical Studies

- The efficacy of Trelegy Ellipta has been evaluated in 3 clinical trials
  - **Trials 1 and 2** were multicenter, randomized, double-blind, parallel-group, 12-week treatment trials in which patients were coadministered umeclidinium 62.5mcg + fluticasone furoate/vilanterol 100mcg/25mcg
  - **Trial 3** was a randomized, multicenter, double-blind, parallel-group, 52-week treatment trial that compared the efficacy of Trelegy Ellipta with the fixed-dose combinations of fluticasone furoate/vilanterol 100mcg/25mcg and umeclidinium/vilanterol 62.5mcg/25mcg

Clinical Studies

- **Trials 1 and 2:**
  - The **primary endpoint** was change from baseline in trough FEV_1 at Day 85
  - In both trials, umeclidinium + fluticasone furoate/vilanterol showed a **statistically significant increase** vs placebo + fluticasone furoate/vilanterol

Clinical Studies

- In **Trial 1** (n=206), the difference from placebo in trough FEV_1 was 124mL (95% CI: 93, 154)
- In **Trial 2** (n=206), the difference from placebo in trough FEV_1 was 122mL (95% CI: 91, 152)
- Secondary endpoints showed similar results for the weighted mean FEV_1 (0–6 hours postdose) on Day 84

Clinical Studies

- In both trials, patients treated with umeclidinium + fluticasone furoate/vilanterol on average **used less rescue medication** vs patients treated with placebo + fluticasone furoate/vilanterol over Weeks 1 to 12

Clinical Studies

- Health-related quality of life was assessed using the SGRQ
- Responder rate was defined as a decrease in score from baseline ≥4 at Day 84
  - **Trial 1:** 40% for umeclidinium + fluticasone furoate/vilanterol vs 35% for placebo + fluticasone furoate/vilanterol (odds ratio 1.2, 95% CI: 0.8, 1.8)
  - **Trial 2:** 35% vs 21% (odds ratio 2.0, 95% CI: 1.3, 3.1)

Clinical Studies

- **Trial 3**
  - Treatment with Trelegy Ellipta showed a statistically significant improvement in lung function (mean change from baseline trough FEV_1 at Week 52) vs fluticasone furoate/vilanterol and umeclidinium/vilanterol
  - Mean change from baseline in trough (predose) FEV_1 at Week 52 was 97mL for Trelegy Ellipta vs fluticasone furoate/vilanterol (95% CI: 85, 109; *P*<.001) and 54mL for Trelegy Ellipta vs umeclidinium/vilanterol (95% CI: 39, 69; *P*<.001)

Clinical Studies

- The primary endpoint was **annual rate of on-treatment moderate and severe exacerbations**
  - Treatment with Trelegy Ellipta statistically significantly reduced the on-treatment annual rate of moderate/ severe exacerbations by 15% vs fluticasone furoate/ vilanterol and by 25% vs umeclidinium/vilanterol
  - Treatment with Trelegy Ellipta statistically significantly decreased the risk of a moderate/severe exacerbation as measured by time to 1st exacerbation vs fluticasone furoate/vilanterol (14.8%; 95% CI: 9.3, 19.9; *P*<.001) and umeclidinium/vilanterol (16.0%; 95% CI: 9.4, 22.1; *P*<.001)

Clinical Studies

- Treatment with Trelegy Ellipta reduced the on-treatment annual rate of severe exacerbations by 13% vs **fluticasone furoate/vilanterol** (95% CI: -1, 24; *P*=.064) (not statistically significant)
- Treatment with Trelegy Ellipta statistically significantly reduced the on-treatment annual rate of severe exacerbations by 34% compared with **umeclidinium/vilanterol** (95% CI: 22, 44; *P*<.001)

- For more clinical trial data, see the prescribing information for Trelegy Ellipta

New Product Monograph

- For more information view the product monograph available at:

http://www.empr.com/trelegy-ellipta/drug/34772/