HAUTE AUTORITÉ DE SANTÉ

CHEST MEDICINE
New medicinal product
March 2018

TRANSPARENCY COMMITTEE OPINION SUMMARY

TRELEGY ELLIPTA / ELEBRATO ELLIPTA *

(fluticasone / umeclidinium / vilanterol), inhaled corticosteroid (CSI) combination, long-acting beta-2 agonist (LABA) bronchodilator and long-acting muscarinic antagonist (LAMA) bronchodilator

Low clinical benefit in the management of severe chronic obstructive pulmonary disease (COPD) in adults unsatisfactorily treated with an inhaled corticosteroid and long-acting beta-2 agonistic bronchodilator and no demonstrated benefit in the therapeutic strategy.

Clinical benefit insufficient to justify its reimbursement in the management of moderate COPD.

Main points

- TRELEGY ELLIPTA has been granted marketing authorisation for the continuous treatment of moderate to severe chronic obstructive pulmonary disease (COPD) in adult patients treated unsatisfactorily with a CSI-LABA combination.
- It simplifies the treatment of patients with severe disease, requiring inhaled tritherapy combining long-acting bronchodilators (LABA + LAMA) with a CSI.
- TRELEGY ELLIPTA was statistically superior to the budesonide/formoterol (CSI + LABA) and fluticasone/vilanterol (CSI + LABA) combinations on FEV1, quality of life and the occurrence of exacerbations, though the differences were modest.

Therapeutic strategy

- In all patients, as soon as COPD was diagnosed by a respiratory functional test (FEV1/CV <0.70), physical activity is recommended and a help with quitting smoking is advisable.
- In the event of daily dyspnoea and/or exacerbations, the first-line treatment is long-acting bronchodilator (LABA or LAMA) monotherapy.
- If symptoms persist, despite correctly implemented treatment, bitherapy may be offered. This bitherapy is based on the combination of two long-acting bronchodilators (LABA + LAMA) in patients whose primary symptom is dyspnoea, or exacerbations associated with dyspnoea (mMRC ≥2). In patients with exacerbations, but with no associated significant dyspnoea, the combination of a CSI with a LABA may be considered.
- Tritherapy (LABA + LAMA + CSI) is indicated if exacerbations persist, despite the bitherapy.
- In all cases, a clinical and functional analysis is offered 1 to 3 months after changing the treatment, then every 3 to 12 months, depending on the severity of the COPD.
- **Role of the medicinal product in the therapeutic strategy**
  TRELEGY ELLIPTA is a fixed combination representing a therapeutic alternative in patients with severe COPD, treated unsatisfactorily with a CSI + LABA combination.
  TRELEGY ELLIPTA has no role in the management of moderate COPD.

Clinical data

* The pharmaceutical company also applied for reimbursement of the same combination under a different name, ELEBRATO ELLIPTA. TRELEGY ELLIPTA is mentioned in this document for clarification.

- In the three studies that evaluated the efficacy of TRELEGY ELLIPTA, the patients had moderate to severe bronchostenosis (FEV1/FVC ratio < 0.7), with a CAT symptom score ≥10.
  Based on the FEV1, quality-of-life and moderate to severe exacerbations endpoints, TRELEGY ELLIPTA was statistically superior to a budesonide/formoterol (ICS + LABA) combination in a 24-week study and statistically superior to a fluticasone/vilanterol (ICS + LABA) combination, and to a umeclidinium/vilanterol (LABA + LAMA) combination in a 52-week study.
  The differences observed in these studies, however, were modest.
  TRELEGY ELLIPTA was non-inferior to a triple combination, comprised of a fluticasone/vilanterol 92/22 µg fixed dose combination (CSI/LABA), along with the separate administration of umeclidinium 55 µg (LAMA), on FEV1 in a 24-week study.
- The safety profile of the fluticasone/umeclidinium/vilanterol combination is consistent with that known of the three active principles of this combination. The adverse events most frequently reported during clinical trial with TRELEGY ELLIPTA were rhinopharyngitis (7%), headache (5%) and upper respiratory tract infections (2%). No unexpected adverse events were reported.

Special prescription requirements

- The Transparency Committee recommends that the initial prescription be issue by pneumologists only.

Benefit of the medicinal product

- The actual clinical benefit* of TRELEGY ELLIPTA is low in the continuous treatment of severe COPD in adults treated unsatisfactorily by a CSI + LABA combination.
  The actual clinical benefit of TRELEGY ELLIPTA is insufficient in the continuous treatment of moderate COPD.
- TRELEGY ELLIPTA does not provide any clinical added value** (CAV V) in the management of severe COPD.
- Approved for non-hospital pharmacy reimbursement and for hospital management for the continuous treatment of severe COPD only.

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This document was drafted on the basis of the Transparency Committee opinion dated 21 March 2018 (CT-16518)
available at **www.has-sante.fr**

* The actual clinical benefit of a medicinal product (ACB) is its benefit particularly on the basis of its clinical performances and the severity of the disease treated. The HAS Transparency Committee assesses the ACB, which may be high, moderate, low, or insufficient for the medicinal product to be covered by public funding.

** The clinical added value (CAV) consists of the clinical improvement offered by a medicinal product compared to existing treatments. The HAS Transparency Committee assesses the CAV rating from I, major, to IV, minor. A CAV rating of V (equivalent to "no CAV") denotes a "lack of clinical improvement"