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PULMONOLOGY
New medicinal product
September 2019

TRANSPARENCY COMMITTEE OPINION SUMMARY

TRIMBOW (beclometasone / formoterol / glycopyrronium), inhaled corticosteroid (ICS), long-acting beta-2 agonist (LABA) bronchodilator and long-acting muscarinic antagonist (LAMA) bronchodilator combination

Moderate clinical benefit in the treatment of adult patients with severe chronic obstructive pulmonary disease (COPD) who are not adequately treated by a combination of an inhaled corticosteroid (ICS) and a long-acting beta2-agonist (LABA) or a combination of a long-acting beta2-agonist and a long-acting muscarinic antagonist (LAMA) and no demonstrated clinical added value in the care pathway

Insufficient clinical benefit in the treatment of moderate COPD

Key points

- TRIMBOW has an MA for maintenance treatment in adult patients with moderate to severe COPD who are not adequately treated by a combination of an ICS and a LABA or a combination of a LABA and a LAMA.
- It simplifies the treatment of patients with severe disease, requiring triple inhaled therapy combining two long-acting bronchodilators (LABA + LAMA) with an ICS.
- TRIMBOW was statistically superior to an ICS/LABA or LAMA/LAMA combination for the occurrence of exacerbations, the forced expiratory volume per second (FEV_1) and quality of life, but the differences were modest.

Care pathway

- In all patients, as soon as COPD was diagnosed by a pulmonary function test (FEV_1/CV <0.70), physical activity is recommended, as is help with quitting smoking.
  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 well managed treatment, dual therapy may be offered. This dual therapy is based on a 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 an inhaled corticosteroid with a LABA may be considered.
- Triple therapy (LABA + LAMA + ICS) is indicated if exacerbations persist despite dual therapy.
- In all cases, a clinical and functional assessment 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 care pathway**
  TRIMBOW is a therapeutic alternative in patients with severe COPD not adequately treated by a LAMA/LABA or ICS/LABA dual therapy.
  Escalation to ICS/LAMA/LABA triple therapy should be reserved for patients who continue to present exacerbations under LABA/LAMA or ICS/LABA treatment.
  It has no role in the management of moderate COPD.

Clinical data

- In the four studies having assessed the efficacy of TRIMBOW, patients had severe to very severe bronchoconstriction (baseline FEV_1 < 50% the predicted value, FEV_1/FCV ratio < 0.7), a CAT symptom score ≥ 10 and had presented at least one COPD exacerbation in the course of the previous year.
  Two 12-month studies compared TRIMBOW with ICS/LABA and LAMA/LAMA dual therapies (one study versus beclometasone/formoterol and one study versus indacaterol/glycopyrronium). TRIMBOW was statistically superior to dual therapies for the occurrence of moderate to severe exacerbations, FEV_1 and quality of life. However, the efficacy differences observed were modest.
  The other two studies were a 26-week open-label study that demonstrated that non-inferiority of TRIMBOW compared to a triple combination made of a ICS/LABA fixed combination (fluticasone/vilanterol) plus a LAMA (tiotropium) and one 12-week study in which TRIMBOW was superior to tiotropium.
- The safety profile of TRIMBOW is consistent with the known profile for the three active substances in this combination. The most frequently reported adverse reactions during clinical trials were oral candidiasis, muscle spasms and dry mouth. Since TRIMBOW was brought to market, no unexpected adverse reactions have been identified.

Specific prescribing conditions

- The Transparency Commission recommends that initial prescription be reserved for pulmonology specialists only given the risk of misuse of this fixed combination.

Benefit of the medicinal product

- The clinical benefit* of TRIMBOW is moderate for maintenance treatment in adult patients with severe COPD who are not adequately treated by a combination of an ICS and a LABA or a combination of a LABA and a LAMA
  The clinical benefit* of TRIMBOW is insufficient in the maintenance treatment of moderate COPD
- TRIMBOW provides no clinical added value (CAV V) in the management of severe COPD
- Favourable opinion for retail pharmacy and hospital reimbursement in the maintenance treatment of severe COPD only.

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This document was drafted on the basis of the Transparency Committee opinion dated 18 September 2019 (CT-18101 and 17701) available at **www.has-sante.fr**

* The clinical benefit (CB) of a medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the clinical benefit, which may be substantial, moderate, low, or insufficient for the medicinal product to be covered by public funding.

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