HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
16 JUNE 2020

The legally binding text is the original French opinion version

aclidinium bromide / formoterol fumarate dihydrate
DUAKLIR GENUAIR 340 µg/ 12 µg inhalation powder

Reevaluation

Key points

Favourable opinion for reimbursement as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD). The clinical benefit is now moderate, where previously it was insufficient.

What therapeutic improvement?

No clinical added value compared to the other free or fixed long-acting β2-adrenergic agonist (LABA) and long-acting muscarinic antagonist (LAMA) combinations, indicated in adult patients with COPD.

Role in the care pathway?

The diagnosis and management of patients with COPD must include an assessment of the COPD severity stage based on symptoms (chronic cough, dyspnoea on exertion, purulent expectoration, exacerbations) and lung function status.

Quitting smoking is the only measure liable to slow the decline in FEV_1. Influenza vaccination is recommended. To date, no medicinal products have demonstrated an effect on prevention of progression of COPD towards chronic respiratory insufficiency. Cardiorespiratory rehabilitation for exercise leads to an improvement in symptoms, quality of life and participation in activities of daily

living, and helps reduce the incidence of exacerbations. The choice of medicinal treatments depends on the symptoms (dyspnoea, exacerbations).

The medicinal management of COPD, outside of exacerbations, is conducted in steps, depending on the severity stage and the response to treatment. The medicinal products used are aimed at:
- Preventing and controlling symptoms;
- Reducing the frequency and severity of exacerbations;
- Improving quality of life;
- Improving exercise tolerance.

Long-acting β2-adrenergic agonist (LABA) and long-acting muscarinic antagonist (LAMA) bronchodilators are recommended when maintenance symptomatic treatment is required, i.e., when daily incapacitating symptoms persist despite the repeated daily use of a short-acting bronchodilator.

A clinical and functional reassessment is offered 1 to 3 months after the prescription of any new medicinal product, then every 3 to 12 months, depending on the severity of the COPD.

If dyspnoea persists, the combination of a long-acting β2-adrenergic agonist (LABA) and a long-acting muscarinic antagonist (LAMA) may improve lung function (FEV_1), quality of life and dyspnoea and may reduce exacerbations without increasing adverse effects.

In the event of frequent exacerbations despite optimal bronchodilator treatment, a combination of LABA + inhaled corticosteroids (ICS) may be proposed, complying with the FEV_1 levels of the MA, or, in the event of associated dyspnoea (mMRC ≥ 2), a LABA + LAMA combination. Triple therapy (LABA + LAMA + ICS) is indicated if exacerbations persist despite one of these options. If dyspnoea or exacerbations persist despite triple therapy, other treatments should be envisaged (macrolides if exacerbations, low-dose morphine derivatives if refractory dyspnoea, discussion of endobronchial treatments in a specialised centre).

Continuous oxygen therapy is reserved for patients with daytime hypoxaemia (PaO2 ≤ 55 mmHg) observed outside an acute episode despite optimal treatment.

Role of the medicinal product in the care pathway

DUAKLIR GENUAIR, a fixed combination of aclidinium and formoterol, is a second-line treatment in patients with moderate to very severe COPD following an inadequate response to a long-acting bronchodilator used as monotherapy.

COMMITTEE'S CONCLUSIONS

Clinical benefit

◗ COPD leads to disability and a marked deterioration in quality of life and may be life-threatening.
◗ This proprietary medicinal product is a maintenance symptomatic treatment for COPD. It has no impact on the long-term decline of lung function.
◗ The efficacy/adverse effects ratio is modest.
◗ There are medicinal alternatives, in particular free and fixed LABA and LAMA combinations.
◗ This proprietary medicinal product is a second-line treatment.

◗ Public health impact:
Considering:
- the seriousness of COPD,
- its prevalence,
- the partially met medical need,
- the absence of robust data on quality of life,
- the absence of any demonstrated impact on the organisation of care,
- the partial response to the identified need with no demonstrated impact on quality of life,

DUAKLIR GENUAIR (aclidinium/formoterol) is unlikely to have an additional impact on public health.

Given all of these elements, the Committee considers that the clinical benefit of DUAKLIR GENUAIR (aclidinium/formoterol) is moderate in the MA indication.

The Committee issues a favourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the indication "maintenance bronchodilator treatment to relieve symptoms in adult patients with COPD" and at the MA dosages.

Clinical Added Value

Considering:
- **demonstration of the superiority of the efficacy of the aclidinium/formoterol combination compared to aclidinium alone on FEV_1 at 1 hour post-dose (difference of 0.084 L (95% CI [0.051; 0.117]) and compared to formoterol on pre-dose FEV_1 (difference of 0.055 L (95% CI [0.023; 0.088]), interim endpoints, with a modest effect size, below clinical relevance thresholds;**
- **the absence of robust data for the aclidinium/formoterol combination concerning the frequency of exacerbations and dyspnoea (unranked but relevant secondary endpoints);**
- **the absence of demonstration of an improvement in quality of life of the aclidinium/formoterol combination compared to aclidinium alone or compared to formoterol alone;**
- **the partially met medical need, in particular by other fixed or free LABA and LAMA combinations having demonstrated a modest effect on bronchodilation;**

the Transparency Committee considers that DUAKLIR GENUAIR (aclidinium/formoterol) provides no clinical added value (CAV V) compared to other free or fixed long-acting muscarinic antagonist and long-acting β2-adrenergic agonist combinations in the maintenance treatment of COPD symptoms.