HAUTE AUTORITÉ DE SANTÉ

RESPIRATORY MEDICINE
New medicinal product
March 2015

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

STRIVERDI RESPIMAT (olodaterol), bronchodilator

No improvement in clinical benefit demonstrated in obstructive pulmonary disease in comparison with other long-acting bronchodilators

Main points

- STRIVERDI RESPIMAT has a Marketing Authorisation as a maintenance bronchodilator treatment of chronic obstructive pulmonary disease (COPD).
- Its efficacy has been demonstrated versus placebo in terms of change in FEV1 but not in terms of reduction in exacerbations, dyspnoea and improvement in the quality of life.
- There are no data that can be used to rate olodaterol by comparison with other long-acting bronchodilators.

Therapeutic use

- Quit smoking is the only action likely to slow down FEV_1 decline . Reconditioning and chest physiotherapy help to improve symptoms, quality of life and participation in everyday activities.
- No medicines are necessary (except during an exacerbation) in case of simple chronic bronchitis.
- In patients who are not inconvenienced by dyspnoea (mild COPD stage I) every day, the on-demand use of short-acting inhaled bronchodilators is usually sufficient.
- Patients with stage II (moderate) to stage IV (very severe) COPD whose dyspnoea interferes with their everyday activities should be offered basic treatment with a long-acting bronchodilator. Three long-acting beta-2 agonists (formoterol, salmeterol and indacaterol) and two long-acting anticholinergics (tiotropium and glycopyrronium) have a Marketing Authorisation in the symptomatic maintenance treatment of COPD. Their efficacy is similar.
- Inhaled corticosteroids are recommended only when taken together with a long-acting bronchodilator in patients with a predicted FEV_1 < 50% having severe (stage III) to very severe (stage IV) COPD and repeated exacerbations. In France, only inhaled corticosteroids in a fixed-dose combination with a long-acting beta-2 agonist have a Marketing Authorisation in this indication.

- **Role of the medicinal product in the therapeutic strategy**
  STRIVERDI RESPIMAT is a symptomatic maintenance treatment for COPD in patients whose respiratory disorder has become permanent, i.e. when the symptoms persist despite the use of a short-acting bronchodilator.

Clinical data

- The efficacy of olodaterol 5 µg/day has been demonstrated in four randomised double-blind studies versus placebo or versus placebo and formoterol 12 µg 2 times/day, lasting 48 weeks, in patients with moderate to very severe COPD. The patients could take concomitant treatments (short- and long-acting anticholinergics, inhaled corticosteroids, salbutamol). In case of exacerbation or symptoms worsening, patients could be treated with salbutamol, oral corticosteroids, theophylline derivatives and antibiotics.
- These four studies have shown the efficacy of olodaterol 5 µg/day by comparison with placebo on $AUC_{0\text{-}3h}$ (area under the curve for FEV_1 between 0 and 3 hours post-dose) but not on the change in pre-dose FEV_1. The differences observed in terms of pre-dose FEV_1 did not seem to be clinically relevant (< 100 ml). Olodaterol 5 µg/day also showed its efficacy by comparison with placebo in terms of the reduction in the use of rescue medication. There is, on the other hand, no proof of the superiority of olodaterol 5 µg/day by comparison with placebo in terms of the reduction in exacerbations of COPD, the reduction in dyspnoea (non-significant difference versus placebo) or the improvement in the quality of life (difference not clinically relevant) which are clinically relevant criteria.

A post-hoc analysis in patients with no concomitant treatment (the population usually included in studies in COPD) showed a larger effect reaching the clinical relevance threshold of 100 ml with a difference versus placebo of 161 ml in the $AUC_{0\text{-}3h}$ of FEV_1 and of 101 ml in the change in pre-dose FEV_1.

- The data supplied versus active comparator do not allow the role of olodaterol 5 µg/day to be defined by comparison with its comparators.
- In studies, the adverse effects reported with olodaterol were infrequent and non-serious, mainly nasopharyngitis, a feeling of dizziness and rash (≥1/1000 to <1/100). However, the risk of systemic effects, particularly cardiovascular ones, inherent in long-acting beta-2 agonists, must be taken into consideration.

Benefit of the medicinal product

- The actual benefit* of STRIVERDI RESPIMAT is moderate.

STRIVERDI RESPIMAT does not provide clinical added value** (CAV V, absence) by comparison with other long-acting bronchodilators.

- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 18 March 2015 (CT-13785) and is available at **www.has-sante.fr**

* The actual benefit (AB) of a proprietary 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 AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The improvement in actual benefit (IAB) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of IAB on a scale from I (major) to IV (minor). A level V IAB means "no clinical added value".