HAUTE AUTORITÉ DE SANTÉ

RESPIRATORY MEDICINE
Update
March 2017

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

ALFALASTIN (human alpha-1 antitrypsin), proteinase inhibitor

No clinical benefit demonstrated compared to usual treatment of emphysema in alpha-1 antitrypsin deficient patients.

Main points

- ALFALASTIN has a Marketing Authorisation in replacement therapy for adults with severe forms of primary alpha-1 antitrypsin deficiency, phenotype PiZZ or PiSZ, with pulmonary emphysema.
- The treatment is to be implemented as soon as possible after the first signs of emphysema. It is to be continued either continuously, especially in case of highly progressive emphysema, or through discontinuous cycles during episodes of bronchopulmonary infections.
- The clinical relevance of the observed effect on the slowing of the loss of lung parenchymal density with ALFALASTIN compared to placebo cannot be estimated.

Therapeutic use

- Emphysema due to genetic deficiency (autosomal recessive transmission) in alpha-1 antitrypsin (AAT) is a rare form of chronic obstructive pulmonary disease. AAT deficiency, defined by a plasma concentration below 11 µmol/L (0.50 g/L), considered to be a protective threshold, predisposes adults to the development of pulmonary emphysema. Without replacement therapy, the median survival is estimated at 14 years after diagnosis; emphysema represents the leading cause of death.
- Medicinal treatment of patients with emphysema due to AAT deficiency is the same as that of any patient with COPD. It essentially involves bronchodilators and inhaled corticosteroids in fixed combination with long-acting beta-2 agonists in patients at risk of exacerbations.
- AAT replacement is the only specific treatment for AAT deficiency.
- **Role of the proprietary medicinal product in the therapeutic strategy**
  ALFALASTIN is a first-line replacement therapy in its indication.

Clinical data

- A randomised, double-blind study evaluated human alpha-1 antitrypsin versus placebo after 24 months of treatment in 180 AAT deficient patients with moderate to severe emphysema (FEV1 between 35% and 70% of the theoretical value). A 34% slowing in lung parenchymal density loss was demonstrated in patients treated with AAT compared with placebo in the annual change in lung parenchymal density measured at the inspiratory phase favouring AAT compared with placebo (p=0.017) (primary endpoint). However, to date, there is no defined threshold of clinical relevance for lung parenchyma loss.
- This study was followed by a 24-month open-label extension phase during which all patients were treated with AAT, with continued effectiveness of the AAT replacement therapy on the progression of emphysema during the 4 years of treatment. A slowing in lung parenchymal density loss was observed in the patients of the placebo group treated with AAT during the extension phase, comparable with that observed in the group initially treated with AAT.
- The most common adverse events were headache and nausea as well as adverse effects potentially related to progression of the disease (COPD, nasopharyngitis, cough, dyspnoea and upper respiratory tract infections).
- There are no data on the evolution of the quality of life score under treatment with AAT.

Special prescribing conditions

- Medicinal product for hospital prescription

Benefit of the medicinal product

- The actual benefit* of ALFALASTIN is low.
- In view of the severity of the disease, the therapeutic need, the lack of defined threshold of clinical relevance for lung parenchyma loss, it is not possible to estimate the clinical relevance of the observed effect on the slowing in lung parenchymal density loss with alpha-1 antitrypsin compared to placebo. Therefore, ALFALASTIN does not provide clinical added value** (CAV V) compared with the current treatment of alpha-1 antitrypsin deficient patients with emphysema.
- Recommends inclusion on the list of reimbursable products for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 08 March 2017 (CT-15852) and is available at **www.has-sante.fr**

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

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