HAUTE AUTORITÉ DE SANTÉ

PULMONOLOGY
Focus
February 2015

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

ESBRIET (pirfenidone), immunosuppressant

Minor improvement in the treatment of idiopathic pulmonary fibrosis only in patients with FVC ≥ 50% and DL_{CO} ≥ 30%

Main points

- ESBRIET has Marketing Authorisation in the treatment of mild to moderate idiopathic pulmonary fibrosis.
- The efficacy of ESBRIET versus placebo has been demonstrated in an improvement in predicted forced vital capacity: the level of the effect is moderate and its efficacy as regards mortality must be viewed with caution given the numerous methodological limitations.
- It represents only a minor improvement in patients with a forced vital capacity (FVC) ≥ 50% and diffusing capacity for carbon monoxide (DL_{CO}) ≥ 30%.
- Use of ESBRIET necessitates regular monitoring of tolerability and liver enzymes, as well as stopping smoking.

Therapeutic use

- There is currently no cure for idiopathic pulmonary fibrosis (IPF). Pirfenidone is recommended in the treatment of mild to moderate IPF. Corticosteroid therapy or cyclophosphamide can be prescribed in acute fibrosis exacerbations.
- In patients with serious resting hypoxaemia (severe chronic respiratory failure), long-term oxygen therapy is recommended. A pulmonary rehabilitation programme may also be proposed for patients with limited exercise capacity and significant disability. Finally, lung transplantation should be considered in serious forms of the disease or if the disease worsens in patients under 65 years of age.
- The FVC and DL_{CO} must be assessed every 3 to 6 months. In the event of worsening of IPF (10% decrease in FVC and/or 15% decrease in DL_{CO}, criteria associated with an increased risk of mortality), treatment should be re-assessed.
- **Role of the medicinal product in the therapeutic strategy**

Given the lack of consensus on the definition of the stages of disease progression, patients with confirmed IPF likely to benefit from pirfenidone therapy are those satisfying the following respiratory function criteria: predicted FVC ≥ 50% and DL_{CO} ≥ 30%. This treatment should be initiated and supervised by a pulmonologist.

Clinical data

- The efficacy and safety of pirfenidone have been evaluated in a randomised double-blind study versus placebo in 555 patients with a mean age of 68 years. The predicted forced vital capacity (FVCp, primary endpoint) on inclusion was 68% and the diffusing capacity for carbon monoxide (DL_{CO}) was 44%. The distance walked in the 6-minute walk test was between 415 and 420 metres.
- The superiority of pirfenidone over placebo after 52 weeks was demonstrated by the change in FVCp, with a decrease of -6.2 points in the pirfenidone group versus -10.9 in the placebo group, and on the following basis: the FVCp was maintained in 22.7% of patients receiving pirfenidone versus 9.7% of patients on placebo, it decreased by less than 10% in 60.8% and 58.5% of patients respectively in the two groups and a decrease in FVCp of at least 10% or death was recorded in 16.5% of patients receiving pirfenidone versus 31.5% of patients on placebo.
- Pooled analysis of the data from three studies showed an absolute difference in mortality of about 3.5% in favour of the pirfenidone group. The lack of direct demonstration of the homogeneity of the patients in these three studies and of a satisfactory level of statistical power limits the conclusions that can be drawn from these results.

- The most commonly reported adverse events were gastrointestinal disorders (nausea, dyspepsia, diarrhoea), rash, photosensitivity and fatigue.

Special prescribing conditions

- Orphan medicinal product
- Exception drug status
- Medicine for hospital prescription
- Prescription restricted to pulmonologists.

Benefit of the medicinal product

- The actual benefit* of ESBRIET is moderate.
- ESBRIET provides minor clinical added value** (CAV IV) in patients with a confirmed clinical radiological and/or histological diagnosis of idiopathic pulmonary fibrosis who do not smoke and satisfy the following respiratory function criteria: FVC ≥ 50% and DL_{CO} ≥ 30%.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

HAUTE AUTORITÉ DE SANTÉ
This document was created on the basis of the Transparency Committee Opinion of 18 February 2015 (CT-13850) and is available at **www.has-sante.fr**

[i] * 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 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".