BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

OPSUMIT (macitentan), endothelin receptor antagonist

No clinical added value demonstrated in patients with class II or III functional status of pulmonary arterial hypertension by comparison with the available treatments

Main points

- OPSUMIT has Marketing Authorisation, in monotherapy or in combination, for the long-term treatment of adult patients with WHO class II or III functional status of pulmonary arterial hypertension (PAH). Its efficacy has been demonstrated in patients with idiopathic and heritable PAH, associated with connective tissue disorders and associated with corrected simple congenital heart disease.

- A study of morbidity and mortality versus placebo favours macitentan in a combined endpoint linking elements of differing weights. The results are based mainly on the reduction in episodes of exacerbations of PAH. No significant difference in terms of mortality was observed.

Therapeutic use

- In newly diagnosed patients, the initiation of a basic treatment is an option.
- In patients with class II PAH, the following oral treatments are used: endothelin receptor antagonists (ambrisentan, bosentan) or phosphodiesterase inhibitors (sildenafil, tadalafil). If monotherapy fails, a combination of treatments can be considered.
- In patients with class III PAH, endothelin receptor antagonists (bosentan or ambrisentan) and phosphodiesterase inhibitors (sildenafil or tadalafil) or riociguat can be used as first-line oral treatment. They are sometimes combined.
- As second-line therapy (due to contraindication, hepatic intolerance to bosentan or failure of oral treatments), prostacyclin analogues are recommended:
  - inhaled iloprost
  - intravenous epoprostenol as a continuous infusion
  - subcutaneous treprostinil. The decision to embark on treprostinil therapy must take account of the high probability of it being necessary to persist with continuous subcutaneous infusion in the long term.
- The overall management of PAH combines, among others, anticoagulants, diuretics, oxygen therapy and calcium channel blockers.
- A lung or heart-lung transplant is the treatment of last resort. It is generally considered in patients who have not improved after 3 months of medical treatment.

Role of the medicinal product in the therapeutic strategy

In patients with class II to III functional status of PAH, OPSUMIT, as monotherapy or in combination treatment, is a new alternative to the first-line symptomatic treatments currently available.

Clinical data

- In one study, 742 patients with class II to IV functional status of symptomatic PAH were randomised (1:1:1) to the groups macitentan 3 mg, 10 mg and placebo. The efficacy of macitentan was evaluated in terms of morbidity and mortality (clinical benefit with a significant reduction as regards occurrence of the first morbidity or mortality event). A significant reduction in this combined endpoint was observed in the macitentan 10 mg group by comparison with placebo: 76 events versus 116, p<0.0001. This result is based mainly on the reduction in exacerbations of PAH: 59 events versus 93. No difference was observed in terms of the first mortality event between the macitentan 10 mg and placebo groups: 16 deaths versus 17.

- According to the SPC, the adverse effects most commonly reported were nasopharyngitis (14.0%), headache (13.6%) and anaemia. The severity of most of these adverse effects was mild to moderate. Monitoring of liver function is recommended on initiation of treatment and monthly during treatment.
Special prescribing conditions

- Medicine for hospital prescription.
- Prescription medicine restricted to specialists in pneumology, cardiology or internal medicine.

Benefit of the medicinal product

- The actual benefit* of OPSUMIT is moderate.
- In view of the available clinical data and in the absence of any data versus active comparators, OPSUMIT does not provide a clinical added value** (CAV V, nonexistent) in therapeutic use in the management of patients with WHO class II or III functional status of pulmonary arterial hypertension.
- Recommends inclusion on the list of reimbursable products for hospital use.

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* 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 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”.

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