HAUTE AUTORITÉ DE SANTÉ

CARDIOLOGY
New indication
March 2017

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

VOLIBRIS (ambrisentan), antihypertensive

No clinical benefit demonstrated in patients with functional class II or III pulmonary arterial hypertension by comparison with the available treatments, in combination with tadalafil, as a first-line treatment.

Main points

- VOLIBRIS has marketing authorisation, in combination, in the treatment of pulmonary arterial hypertension (PAH) in adults in functional class II and III (WHO classification).
- The efficacy of the ambrisentan/tadalafil combination was demonstrated in patients not previously treated compared to ambrisentan and tadalafil as a monotherapy, on the reduction of the time until occurrence of the first cardiovascular event, especially hospitalisation for worsened PAH.
- No difference was found in terms of improvement of functional class or mortality compared to ambrisentan and tadalafil as a monotherapy.
- The use of the ambrisentan/tadalafil combination from the outset in functional class II or III should be discussed in regard to the increase of adverse events associated with this combination.

Pre-existing indications*

VOLIBRIS has marketing authorisation in the treatment of PAH in patients in functional class II and III, not otherwise specified, making it available as a monotherapy from the first line.

Therapeutic use

Conventional treatment for PAH combines anticoagulants, diuretics, oxygen therapy and calcium channel blockers.
In patients with class II PAH, endothelin receptor antagonists (ERA) or phosphodiesterase 5 (PDE5) inhibitors, and guanylate cyclase stimulators (GCS), oral treatments, are recommended.
In patients with class III PAH, ERA, PDE-5 and GCS can be used as an oral first-line treatment. In second line, prostacyclin analogues are recommended.
These treatments are offered as monotherapy or in combination.
A lung or heart-lung transplant is the last-resort treatment, in patients not improved after three months of a medical treatment.

Role of the proprietary medicinal product in the therapeutic strategy

The combination of VOLIBRIS with tadalafil in functional class II or III is now possible but should be discussed in regard to the increase of adverse events associated with the combination of these two medicinal products.

Clinical data

- A phase III study involving 500 treatment-naïve patients showed a reduction in the risk of occurrence of a first morbidity-mortality event, mainly the risk of hospitalisation for worsening of PAH, with ambrisentan/tadalafil compared with ambrisentan and tadalafil as a monotherapy, with an HR of approximately 0.5 (0.48 to 0.53 depending on the groups) and 15 to 18 months of follow-up.
  The data suggest the absence of difference in terms of mortality observed, change of functional class and difference in terms of improved quality of life.
- The main adverse events observed on ambrisentan/tadalafil were peripheral oedema, arterial hypotension, headaches, nasal congestion and anaemia.

* This summary of opinion does not cover these indications.

Special prescribing conditions

- Orphan medicinal product for hospital prescription, reserved for certain specialists (respiratory medicine, cardiology, internal medicine).

Benefit of the medicinal product

- The actual clinical benefit* of VOLIBRIS is moderate.
- VOLIBRIS does not provide any clinical added value** (CAV V) in the therapeutic strategy for management of patients with functional class II or III pulmonary arterial hypertension who were not previously treated.
- 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 8 March 2017 (CT-15105) and is available at **www.has-sante.fr**

* The actual clinical benefit (ACB) 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 ACB, which can be substantial, moderate, low or insufficient for reimbursement of the medicinal product 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 (equivalent to “no CAV”) means “no clinical added value”.