BREIF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

SIMBRINZA (brinzolamide, brimonidine), glaucoma medicine

No clinical benefit demonstrated in glaucoma by comparison with coadministration of its components individually.

Main points

- SIMBRINZA has Marketing Authorisation in decrease of elevated intraocular pressure (IOP) in adult patients with open-angle glaucoma or ocular hypertension for whom monotherapy provides insufficient IOP reduction.
- Brinzolamide (carbonic anhydrase inhibitor) and brimonidine (alpha-2 adrenergic agonist) are second-line treatments. This medicinal product must therefore be reserved for patients with insufficient reduction of IOP with brinzolamide or brimonidine monotherapy.
- It may be used as a substitution for the coadministration of brinzolamide and brimonidine.

Therapeutic use

- A number of glaucoma eye drops are available in local or systemic forms and acting through different mechanisms:
  - reduced secretion of aqueous humour:
    - betablockers
    - alpha-2 adrenergic agonists
    - carbonic anhydrase inhibitors.
  - increased elimination of aqueous humour:
    - adrenaline and adrenergic compounds
    - miotics and parasympathomimetics
    - prostaglandin analogues.
  The choice is essentially made according to the contraindications and adverse effects of each class of drug.

- Betablocker eye drops and prostaglandin analogues are prescribed as first-line therapy. Several pressure-lowering eye drops may be combined, without exceeding triple therapy as a general rule. For dual therapy, a prostaglandin analogue and a beta-blocker may be combined if one of these has proved to be insufficiently effective or ineffective as first-line monotherapy. The other classes of pressure-lowering eye drops are prescribed:
  - as first-line monotherapy in cases where betablockers and prostaglandin analogues are contraindicated,
  - as a second-line treatment, either as monotherapy or in combination with beta-blockers or prostaglandin analogues, where these are insufficiently effective.
  In some cases that cannot be controlled by eye drops, these may be combined with systemic acetazolamide, a carbonic anhydrase inhibitor. However, the frequent and disabling adverse effects of acetazolamide (metabolic acidosis, hypokalaemia, kidney stones) limit its use.

- In the most serious cases, surgery may be required at the time of diagnosis, but surgery is generally reserved for patients in whom pharmacological treatment has failed. Surgery is the preferred option when the glaucoma is advanced or the patient is young. Laser trabeculoplasty may be used after the failure of medical treatment and before considering another surgical procedure.

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Role of the medicinal product in the therapeutic therapy

Brinzolamide and brimonidine are second-line treatments. SIMBRINZA is therefore a second-line medicinal product in the event of insufficient reduction of IOP by brinzolamide or brimonidine monotherapy or as a substitution for coadministration of brinzolamide and brimonidine.

Clinical data

The efficacy and safety of the brinzolamide 10 mg/ml / brimonidine 2 mg/ml fixed combination were evaluated in two randomised, double-blind studies; one, a superiority study versus the components of the combination in monotherapy and the other, a non-inferiority study versus the coadministration of the components of the combination in adults with open-angle glaucoma or intraocular hypertension inadequately controlled with monotherapy or previously treated with multiple drugs to lower their IOP.

The brinzolamide/brimonidine fixed combination was superior to brinzolamide and brimonidine monotherapy on the change in mean diurnal IOP at 3 months compared with baseline with an IOP reduction of -7.9 mmHg with the brinzolamide/brimonidine combination versus -6.5 mmHg with brinzolamide and -6.4 mmHg with brimonidine i.e. differences in absolute value of 1.4 and 1.5 mmHg, respectively (p < 0.0001). Only the difference versus brimonidine reaches the level of clinical relevance (≥ 1.5 mmHg).

The brinzolamide/brimonidine fixed combination was not inferior to the coadministration of brinzolamide and brimonidine. At 3 months, the change in mean diurnal IOP was -8.5 mmHg in the brinzolamide/brimonidine group and -8.3 in the brimonidine + brinzolamide group, i.e. a difference of -0.1 mmHg with 95% CI = [ 0.5; 0.2]; the upper limit was below the predefined non-inferiority threshold (+1.5 mmHg).

In clinical studies, the safety profile of the brinzolamide/brimonidine fixed combination was similar to that of each of its components taken individually. The most common adverse effects were ocular hyperaemia, ocular allergic-type reactions occurring in approximately 6-7% of patients, and taste perversion (bitter or unusual taste in the mouth following instillation) in approximately 3% of patients.

A risk of systemic adverse effects must be considered in ocular administration of the brinzolamide/brimonidine combination.

Benefit of the medicinal product

The actual benefit* of SIMBRINZA is substantial.
SIMBRINZA does not provide any clinical added value (CAV V, non-existent) compared with the coadministration of its components individually.
Recommends inclusion on the list of reimbursable products for supply by pharmacists and 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 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".