BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

**XALATAN** (latanoprost), glaucoma eye drops

**No demonstrated clinical benefit in the reduction of elevated intraocular pressure in children**

**Main points**

- **XALATAN now has marketing authorisation in reduction of elevated intraocular pressure in paediatric patients with elevated intraocular pressure (IOP) and paediatric glaucoma.**
- A randomised clinical study demonstrated its non-inferiority relative to timolol on mean reduction of intraocular pressure IOP after 12 weeks of treatment.
- **XALATAN contains benzalkonium chloride in its formulation and no long-term safety data are available.**
- **XALATAN, like other eye drops, can be useful short-term, while awaiting surgery, or as an additional treatment with surgery whose result is insufficient, as well as long-term in other less aggressive forms of paediatric glaucoma.**

**Pre-existing indications**

- **XALATAN already had marketing authorisation in the treatment of reduction of elevated intraocular pressure in patients with open angle glaucoma and ocular hypertension.**

**Therapeutic use**

- Outside of congenital glaucoma, there are many situations where medical treatment is prescribed first line because the seriousness of the initial clinical presentation does not justify surgery right away.
- **Only travoprost and latanoprost, prostaglandin analogues, specifically have marketing authorisation in children in the reduction of elevated IOP and paediatric glaucoma. Data are nevertheless available for certain eye drops of the classes of beta-blockers (timolol) and carbonic anhydrase inhibitors (dorzolamide and brinzolamide). These eye drops are often used in combination, in medical practice.**
- Brimonidine (ALPHAGAN) and apraclonidine (IOPIDINE) are not recommended in children due to the risk of adverse events reported in several studies.
- **XALATAN contains benzalkonium chloride and preservatives present in multi-dose eye drops can induce inflammatory conjunctival adverse effects and toxicity of the eye surface.**
- **Role of the medicinal product in the therapeutic strategy**

In the majority of congenital glaucoma cases, due to the urgency of care, the first-line treatment is surgical. Latanoprost, like other eye drops, can be useful short-term, while awaiting surgery, or as an additional treatment with surgery whose result was insufficient.

In other less-aggressive forms of paediatric glaucoma, latanoprost is a first-line treatment which can be prescribed long-term like other eye drops.

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1 This summary does not cover these indications.
Clinical data

- The efficacy data for latanoprost in children rely on a non-inferiority study that compared latanoprost 0.005% once daily to timolol 0.5% (or optionally timolol 0.25% for patients below age 3 years) twice daily for 12 weeks in 137 patients below 18 years of age. Timolol does not have specific paediatric marketing authorisation even though efficacy data are available. Patient characteristics were similar between the groups, with a mean age of 9 years and mean baseline IOP comprised between 27.3 and 27.8 mmHg.

- After 12 weeks of treatment and relative to baseline, the mean IOP reduction (primary endpoint) was 7.2 mmHg in the latanoprost group and 5.7 mmHg in the timolol group, or a difference of 1.46 mmHg (95% CI [-0.81; 3.74]). Since the lower 95% CI bound was greater than the predefined non-inferiority bound of -3 mmHg, the non-inferiority of latanoprost relative to timolol could be concluded in the per-protocol population (n=107).

- The marketing authorisation for travoprost, the only comparator to have marketing authorisation that overlaps with latanoprost, is based on comparable results of a clinical study that demonstrated the non-inferiority of travoprost 0.004% once daily versus timolol 0.5% twice daily in 152 paediatric patients.

- The safety profile for XALATAN was comparable to that observed in adults and no new adverse reactions were identified. The most commonly reported adverse events (>5% in one of the two groups) were nasopharyngitis and headaches.

Benefit of the medicinal product

- The actual benefit* of XALATAN is substantial.

- XALATAN provides no clinical added value (CAV V) in the treatment strategy for managing paediatric patients with elevated intraocular pressure with paediatric glaucoma that includes surgery and glaucoma eye drops (travoprost, timolol, dorzolamide and brinzolamide) given:
  - the demonstration of the non-inferiority of latanoprost relative to timolol after 12 weeks of treatment on the reduction of intraocular pressure in children,
  - the absence of long-term safety data for latanoprost.

- 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".