HAUTE AUTORITÉ DE SANTÉ

ENT
Update
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SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

CILOXADEX (ciprofloxacin, dexamethasone), anti-infective and corticosteroid

Low clinical interest for cases of otorrhoea after grommet insertion

Main points

- CILOXADEX has been granted a marketing authorisation for the treatment of otorrhoea after grommet insertion in adults and children.
- Fluoroquinolone ear drops are the first-line antibiotics for otorrhoea after grommet insertion
- The benefit of combining a corticosteroid with the topical antibiotic has not been demonstrated; hence, CILOXADEX is a second-line treatment.

Pre-existing indication*

CILOXADEX has also been granted a marketing authorisation for the treatment of acute otitis externa in adults and children.

Therapeutic strategy

- For cases of otorrhoea after grommet insertion, the first-line local antibiotic therapy is based on a fluoroquinolone (ciprofloxacin or ofloxacin). Rifamycin has also been granted a marketing authorisation for this indication, but it is ineffective against *Pseudomonas aeruginosa* with frequent clinical and microbiological failures. It is used as a second-line treatment after antibiotic susceptibility testing.
- **Role of the medicinal product in the therapeutic strategy**
  CILOXADEX is a fixed combination of ciprofloxacin and dexamethasone. Adding dexamethasone to an antibiotic could enable more rapid drainage of otorrhoea than the topical antibiotic alone; however, the benefit of such an effect is not established and the risk associated with the corticosteroid (decrease in immune response, masking of clinical signs of infection) is not ruled out. Hence, CILOXADEX is a second-line treatment.

Clinical data

- In a single-blind, randomised study, on patients aged from 6 months to 12 years (mean 2.4 years), having acute otitis media with otorrhoea after grommet insertion, the fixed ciprofloxacin/dexamethasone combination (4 drops twice-daily, for 7 days) was non-inferior to ofloxacin 0.3% (5 drops twice-daily, for 10 days). The clinical recovery percentage was 87.9% versus 77.3% and the bacteriological eradication percentage was 71.1% versus 63.2%. However, the dose of ofloxacin (5 drops twice-daily) administered in this study was lower than that of its French marketing authorisation (10 drops twice-daily), which limits the transferability of the findings of this study to French practice. Failing a group treated with ciprofloxacin alone, this study is not suitable for assessing the added value of dexamethasone over the efficacy observed with the fixed ciprofloxacin/dexamethasone combination.

- In a randomised phase II study, the fixed ciprofloxacin/dexamethasone combination (3 drops twice-daily) was compared, in single-blind mode, to ciprofloxacin (3 drops twice-daily) for 7 days. The mean period required to

* This summary does not concern this indication.

eradicate otorrhoea was shorter with the fixed ciprofloxacin/dexamethasone combination than with ciprofloxacin (4.1 vs 5.4 days; $p < 0.001$), but this difference is of little clinical relevance.

- No serious systemic or ear-related adverse effect associated with CILOXADEX was reported in the clinical studies.
  A warning was included in the SPC, stating that corticosteroids may lower the immune response and thereby promote the onset of bacterial, viral or fungal infections. They may mask the clinical signs of an infection, preventing detection of antibiotic inefficacy; they may also suppress hypersensitivity reactions to the substances present in the medicinal product (See section 4.4. of SPC).

Benefit of the medicinal product

- The actual clinical benefit* of CILOXADEX is low
- Approval for retention of non-hospital pharmacy reimbursement and for hospital treatment.

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This document was drafted on the basis of the Transparency Committee opinion dated 07 March 2018 (CT-16682) available at **www.has-sante.fr**

* The actual clinical benefit of a medicinal product (ACB) consists of its benefit particularly on the basis of its clinical performances and the severity of the disease treated. The HAS Transparency Committee assesses the ACB, which may be high, moderate, low, or insufficient for the medicinal product to be covered by public funding.