HAUTE AUTORITÉ DE SANTÉ

ENT
Update
November 2017

SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

Anti-infectives combined with a corticosteroid in ear drop solution:
ANTIBIO SYNALAR (neomycin, polymyxin B, fluocinolone)
AURICULARUM (oxytetracycline, polymyxin B, nystatin, dexamethasone)
CILOXADEX (ciprofloxacin, dexamethasone)
FRAMYXONE (framycetin, polymyxin B, dexamethasone)
PANOTILE (polymyxin B, neomycin, fludrocortisone, lidocaine)
POLYDEXA (neomycin, polymyxin B, dexamethasone)

Low clinical benefit for the treatment of acute otitis externa

Main points

- These medicinal products have been granted a marketing authorisation for the topical treatment of bacterial acute otitis externa. Proprietary medicinal products containing an amino sugar (ANTIBIO SYNALAR, FRAMYXONE, PANOTILE and POLYDEXA) are restricted to the treatment of acute otitis externa with a closed tympanum. Also, AURICULARUM has also been granted a marketing authorisation for the topical treatment of bacterial and/or fungal acute otitis externa.
- The efficacy in obtaining clinical recovery from acute otitis externa is not the subject of relevant evidence for these fixed antibiotic + corticosteroid combinations, with the exception of CILOXADEX.
- The benefit of combining a corticosteroid with the topical antibiotic treatment for the treatment of acute otitis externa has not been demonstrated for any of these medicinal products.
- Given the long follow-up period of use in particular, the higher risk of antibiotic resistance with fluoroquinolones and the lack of alternatives containing a non-fluoroquinolone antibiotic and not combined with a corticosteroid, they retain a low clinical benefit.
- CILOXADEX should be used as a second-line treatment due to the higher risk of antibiotic resistance with fluoroquinolones or in cases of an open tympanum or previous history of tympanic perforation. The role of AURICULARUM in the therapeutic strategy for otitis externa is limited; it should be reserved for acute otitis externa of fungal or combined fungal and bacterial origin.

Pre-existing indications*

CILOXADEX: treatment of otorrhoea after grommet insertion
AURICULARUM: topical treatment of chronic otitis for pre-operative draining and for post-operative use in the petromastoid canal, in cases of secondary infection.

Therapeutic strategy

- Antibiotic ear drops are the basic treatments for acute otitis externa of bacterial origin. Acute otitis externa of fungal origin should be treated with an antifungal. Antibiotics are of no benefit for fungal otitis externa. Otitis

* This summary does not concern these indications.

externa is of bacterial origin in 90% of cases (*Pseudomonas aeruginosa* or *Staphylococcus aureus*) and fungal in 10% of cases (*Aspergillus*).
The diagnosis should be established on the basis of a patient interview and thorough otoscopic examination of the ear canal in order to differentiate a bacterial or fungal cause of the infection, rule out other causes of earache and inflammation of the external ear canal not requiring antibiotic treatment and also establish whether the tympanum is closed or open so as not to prescribe ototoxic amino sugar antibiotics if the tympanum is open. Fluoroquinolones are prescribed for patients having known perforation or previous history indicating perforation.
Systemic antibiotic therapy is reserved for severe forms (perichondritis and chondritis).

- Atraumatic cleaning of the external ear canal should be carried out if possible. In the event of narrowing of the ear canal, it is recommended to insert an expandable plug into the canal to enable satisfactory penetration of the drops and retain a high local antibiotic concentration.
- It is recommended to assess pain and treat it according to its severity. The pain experienced with acute otitis externa may be significant and its intensity is frequently underestimated by the physician. Pain of minor to moderate intensity generally responds to oral paracetamol or NSAID treatment.
- **Role of the medicinal products in the therapeutic strategy**
  ANTIBIO SYNALAR, FRAMYXONE, PANOTILE and POLYDEXA, containing an amino sugar, are first-line treatments for acute otitis externa of bacterial origin with a closed tympanum.
  CILOXADEX, containing a fluoroquinolone, should be used as a second-line treatment or for cases of known tympanic perforation or previous history indicating perforation.
  AURICULARUM is a second-line treatment to be reserved for acute otitis externa of fungal or combined bacterial and fungal origin.

Clinical data

No clinical data demonstrating the efficacy of ANTIBIO SYNALAR and FRAMYXONE in acute otitis externa are available.
The studies conducted with PANOTILE are old, of poor methodological quality and have not studied the efficacy of PANOTILE specifically in acute otitis externa.
POLYDEXA was assessed in a comparative clinical study versus acetic acid as monotherapy or in combination with dexamethasone which are not available treatments in France.
CILOXADEX has demonstrated its efficacy in acute otitis externa versus CILOXAN (containing no corticosteroid) and an amino sugar/polypeptide/corticosteroid combination but has not demonstrated its superiority over CILOXAN in respect of pain.
No data are available demonstrating the benefit of combining a corticosteroid or an anaesthetic with a local antibiotic.

Benefit of the medicinal product

- The actual clinical benefit* of these proprietary medicinal products 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 9 November 2017 (CT-15316-16190-16233-15333-15401-15457 and 16255) 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.