Therapeutic Class Overview
Otic Fluoroquinolones

Therapeutic Class

- **Overview/Summary:** This review will focus on the otic fluoroquinolone antibiotics.[1-6] Topical corticosteroids help to aid in the resolution of the inflammatory response accompanying bacterial infections. Fluoroquinolones are broad-spectrum antimicrobial agents that directly inhibit bacterial deoxyribonucleic acid (DNA) synthesis by blocking the actions of DNA gyrase and topoisomerase IV, which leads to bacterial cell death.[1-6]

  The otic antibacterials are approved for the treatment of otitis externa and otitis media. Otitis externa (also known as swimmer's ear) is an inflammatory condition of the external ear canal auditory canal or auricle, usually from infection. Common infectious pathogens include S. aureus, S. epidermidis and P. aeruginosa; however, several other gram-positive, gram-negative and anaerobic infections along with polymicrobic infections occur frequently.[8] Topical antibacterials (alone or in combination with a corticosteroid) are very effective and systemic therapy is generally not required.[9] Acute otitis media is an inflammatory condition of the middle ear with middle ear effusion and symptoms include otalgia, hearing loss and vertigo.[10] Common pathogens in children include S. pneumoniae and H. influenzae (and M. catarrhalis in children).[10,11] Oral antibacterials are generally the initial treatment option for children and adults; however, topical antibacterials with or without corticosteroids may be used in patients with perforated tympanic membranes, tympanostomy tubes or chronic suppurative otitis media.[11-14] Current clinical guidelines support these recommendations.[15-19]

  This review only includes otic dosage forms.

Table 1. Medications Included Within the Therapeutic Class Review[4-12]

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Second Generation Fluoroquinolones			
Ciprofloxacin (Cetraxal®*, Otiprio®)	Treatment of acute otitis externa (Cetraxal®)#, bilateral otitis media with effusion in pediatric patients six months of age or older undergoing tympanostomy tube placement (Otiprio®)	Otic solution, single use container (Cetraxal®): 0.2% Otic suspension (Otiprio®) 6%	✔
Ofloxacin*	Treatment of acute otitis externa‖, treatment of chronic suppurative otitis media with perforated tympanic membranes†, acute otitis media in pediatric patients with tympanostomy tubes‡	Otic solution: 0.3%	✔
Third Generation Fluoroquinolones			
Ciprofloxacin/ dexamethasone (Ciprodex®)	Treatment of acute otitis externa§, acute otitis media in pediatric patients with tympanostomy tubes‡	Otic suspension: 0.3%/0.1%	-
Ciprofloxacin/ fluocinolone (Otovel®)	Acute otitis media with tympanostomy tubes**	Otic solution: 0.3%/0.025%	
Ciprofloxacin/ hydrocortisone (Cipro HC®)	Treatment of acute otitis externa¶	Otic suspension: 0.2%/1%	-

*Generic is available in at least one dosage form or strength.
‖For adult and pediatric patients, ≥6 months of age, due to susceptible strains of E. coli, P. aeruginosa and S. aureus.
†For adult and pediatric patients ≥12 years of age, due to susceptible strains of P. mirabilis, P. aeruginosa and S. aureus.

‡For pediatric patients ≥1 year of age, due to susceptible strains of H. influenzae, M. catarrhalis, P. aeruginosa, S. aureus and S. pneumoniae.
§For adult and pediatric patients ≥6 months of age, due to susceptible strains of S. aureus and P. aeruginosa.
¶For adult and pediatric patients ≥1 year of age, due to susceptible strains of P. aeruginosa, S. aureus, and P. mirabilis.
#For adult and pediatric patients ≥1 year of age, due to susceptible strains of P. aeruginosa and S. aureus.
**For pediatric patients ≥6 months of age, due to susceptible strains of six months of age or older H. influenzae, M. catarrhalis, P. aeruginosa, S. aureus and S. pneumoniae.

Evidence-based Medicine

- Clinical trials have demonstrated that otic fluoroquinolones are effective in treating and providing relief of in otitis externa, chronic suppurative otitis media with a perforated tympanic membrane, bilateral otitis media with effusion, and acute otitis media in patients with tympanostomy tubes.[20-33]
- For otitis externa, ciprofloxacin/dexamethasone has been shown to have significantly greater clinical and microbial cure (P=0.0375 and P=00375 respectively), pain relief (P=0.0013), time to cure (no P value given) and eradication of (P=0.0044) when compared to hydrocortisone/neomycin/polymyxin B.[20-23]
- The other otic quinolones, ciprofloxacin (Cetraxal®), ofloxacin, ciprofloxacin/hydrocortisone and ciprofloxacin/dexamethasone all showed non-inferiority to hydrocortisone/neomycin/polymyxin B in the treatment of otitis externa.[24-27]
- In the treatment of otitis media, ciprofloxacin and ofloxacin have both been shown to be non-inferior to other therapies.[29,30]
- Ciprofloxacin/dexamethasone has shown significantly better clinical cure rates and time to cessation of otorrhea when compared to oral amoxicillin/clavulanate, otic ciprofloxacin alone and otic ofloxacin.[31-33]
- Ciprofloxacin 6% (Otiprio®) was evaluated in two unpublished, randomized, multicenter controlled clinical trials with a total of 532 pediatric patients for the treatment of bilateral otitis media with effusion undergoing myringotomy with tympanostomy tube placement. Differences in treatment failure between the ciprofloxacin 6% group and the sham group was 20% (95% CI, 8 to 32%) and 24% (95% CI, 12 to 36%) for trials one and two, respectively (P<0.001 for both comparisons).[2]
- The safety and efficacy of ciprofloxacin/fluocinolone otic solution for the treatment of acute otitis media with tympanostomy tubes was established in two unpublished multicenter, randomized, double-blind, active-controlled, parallel group trials. In trail 1, median time to cessation of otorrhea was significantly reduced with combination ciprofloxacin/fluocinolone (3.75 days) when compared to ciprofloxacin monotherapy (7.69 days; P=<0.001) and fluocinolone monotherapy (not estimable; P<0.001). In trail 2, median time to cessation of otorrhea was significantly reduced with combination ciprofloxacin/fluocinolone (4.94 days) when compared to ciprofloxacin monotherapy (6.83 days; P=0.028) and fluocinolone monotherapy (not estimable; P<0.001).[5]

Key Points within the Medication Class

- According to Current Clinical Guidelines:[15-19]
    - Topical therapy, without systemic antibiotics, should be used for initial management of uncomplicated acute otitis externa in otherwise healthy patient with diffuse acute otitis externa that is not complicated by osteitis, abscess formation, middle ear disease, or recurrent episodes of infection.
    - For otic antibiotics, due to lack of differences in efficacy, the cost, adherence to therapy, and adverse effects of topical antimicrobials must also be considered.
    - When the patient has a known or suspected perforation of the tympanic membrane in otitis externa, including a tympanostomy tube, the clinician should prescribe a non-ototoxic topical preparation.
    - In otitis media, otic antibiotics should be used first line in patients with tympanostomy tubes, otherwise oral antibiotics are recommended first line (amoxicillin ± clavulanic acid).
- Other Key Facts:
    - Ciprofloxacin (Cetraxal®), ofloxacin and ciprofloxacin/fluocinolone are all formulated as solutions, whereas ciprofloxacin (Otiprio®), ciprofloxacin/dexamethasone and ciprofloxacin/hydrocortisone are formulated as suspensions.. [1-6]

- Depending on type of infection and selected agent, typical administration is three to 10 drops once or twice daily for seven to 14 days. [1-6]
- Each agent can be given to pediatric patients, but the age differs for each product. [1-6]
- Currently only ciprofloxacin (Cetraxal®) and ofloxacin otic solutions are available generically.

References

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