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AWMSG Secretariat Assessment Report – Limited submission

Ciprofloxacin (Cetraxal®) 2 mg/ml ear drops solution in single-dose container

Company: Aspire Pharma Ltd

Licensed indication under consideration: Treatment of acute otitis externa in adults and children older than 1 year with an intact tympanic membrane, caused by ciprofloxacin susceptible microorganisms

Marketing authorisation date: 14 January 2011
UK launch date: 12 January 2018

Comparator(s)

The company suggests that ciprofloxacin would be prescribed in people with acute otitis externa that either have a sensitivity to neomycin and/or steroids, have suspicion of a perforated eardrum, or do not require steroids. Therefore, the comparators included in the company submission are:

- chloramphenicol 5% and 10%
- off-label/unlicensed ofloxacin
- unlicensed ciprofloxacin.

Limited submission details

- Anticipated usage in NHS Wales is considered to be of minimal budgetary impact.

Clinical effectiveness

- Ciprofloxacin (Cetraxal®) is the first licensed ciprofloxacin product indicated for acute otitis externa. Welsh prescribing data indicates that approximately 70 people were prescribed unlicensed ciprofloxacin in 2017.
- Welsh primary care antimicrobial prescribing guidelines recommend aural toilet (if available) and analgesia for acute otitis externa. If needed, treatment with over-the-counter acetic acid 2% or neomycin with a steroid is recommended.
- The National Institute for Health and Care Excellence (NICE) clinical knowledge summary for acute diffuse otitis externa states that there is no evidence to suggest which product is more effective for acute otitis externa; factors such as the person's preference, risk of adverse effect, cost, dosing frequency and status of the eardrum should be taken into account. The clinical knowledge summary also highlights that chloramphenicol may cause contact dermatitis in up to 10% of patients due to the presence of propylene glycol.
- Efficacy and safety of ciprofloxacin was investigated in one pivotal multicentre study (CIPROT III), which the company states formed part of the evidence for licensing. The study showed that ciprofloxacin is non-inferior to the combination product polymyxin B, neomycin and hydrocortisone in patients aged at least two

years old who had acute diffuse otitis externa. The company provided other studies that were supportive of these results.
- Clinical expert opinion sought by AWTTC suggests that the less frequent dosing interval (twice daily) of ciprofloxacin may lead to increased compliance and convenience versus aminoglycosides such as neomycin and gentamicin, which are dosed 3–4 times daily.
- The safety and efficacy of Cetraxal® has not been studied in the presence of a perforated tympanic membrane.

Budget impact

- Based on complete displacement of the suggested comparators, the company estimates that a total of 225 people will be eligible for ciprofloxacin (Cetraxal®) in Wales per year. This is based on 2016 Welsh prescription cost analysis data for chloramphenicol, ofloxacin and unlicensed ciprofloxacin.
- The company estimates that the number of patients receiving ciprofloxacin (Cetraxal®) will be 75 patients in Year 1, rising to 225 patients in Year 5. This is based on the assumption that unlicensed ciprofloxacin and ofloxacin will be completely displaced in the first year. The company expects that Cetraxal® will gradually displace chloramphenicol, with complete replacement by Year 5. Overall, this results in a cost saving of £8,919 in Year 1, increasing to a cost saving of £17,401 in Year 5.
- Clinical expert opinion sought by AWTTC suggests that in addition to the displacement of chloramphenicol, ofloxacin and unlicensed ciprofloxacin, some displacement of neomycin and steroids may occur. Therefore, the company's estimate of 225 people eligible per year would be a significant underestimate. The company acknowledges that some displacement of other products, including aminoglycosides, may occur; however, the company suggests such displacement would be minimal. In a sensitivity analysis, the company considers partial displacement (26%) of other products in addition to the 100% displacement of unlicensed ciprofloxacin, ofloxacin and chloramphenicol. This leads to a total cost saving of £103 per year.

Additional information

- AWTTC is of the opinion that, if recommended, ciprofloxacin (Cetraxal®) may be appropriate for prescribing by all prescribers within NHS Wales for the indication under consideration.

Evidence search

Date of evidence search: 7 and 8 March 2018
Date of range of evidence search: No date limits were applied to database searches.

Further information

This assessment report will be considered for review every three years.
References are available on request. Please email AWTTC at AWTTC@Wales.nhs.uk for further information.

This report should be cited as: All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report. Ciprofloxacin (Cetraxal®) 2 mg/ml ear drops solution in single-dose container. Reference number: 1343. May 2018.