VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Otitis externa (also known Swimmer's ear) is an inflammation or infection of the external ear canal and the outer ear, usually due to bacteria such as streptococcus, staphylococcus, or pseudomonas. OE is one of the most frequent conditions found in the offices of ear, nose and throat specialists and GPs, accounting for 3% to 10% of patients.

The infections of the outer ear can be classified according to their aetiology, localisation and evolution. The treatment depends on a correct diagnosis based on knowledge of the anatomy and the physiology of the external ear canal (EEC) and the microbiology and the clinical manifestations presented by the patient. To control the infection, the EEC should be cleaned so that topical treatment can reach the infection and be effective.

Acute otitis media (AOM) is an inflammation of the middle ear that usually results from infection. When fluid accompanies the inflammation, the condition is known as otitis media with effusion. The most common surgery performed in children for treatment of recurrent otitis media with effusion is the insertion of a tympanostomy tube into the eardrum. In the US, approximately two million tympanostomy tubes are inserted annually. With the tympanostomy tube in place, the middle ear is accessible to topical medications applied to the external auditory canal.

The most common complications reported after tube insertion include otorrhea, the formation of granulation tissue around the tube, and cholesteatoma. The estimated incidence of AOM accompanied by otorrhea in patients with tympanostomy tubes ranges from 10% to 20%. Many practitioners use topical antibiotics to treat children who have Acute Otitis Media with Tympanostomy Tubes (AOMT).

VI.2.2 Summary of treatment benefits

Two studies were carried out by SALVAT to investigate Cetraxal Plus in the treatment of otitis externa and 2 other studies were carried out in the treatment of otitis media. The results from these studies demonstrated that Cetraxal Plus has good efficacy and safety profile in both indications.

In the first study in otitis externa, 95 patients under Cetraxal Plus treatment and 97 patients under control treatment were included. The percentage of recovery from ear pain, ear swelling and discharge from the ear was greater in the Cetraxal Plus group. There was a trend toward statistical significance for the investigator evaluation and the bacteriological results in favour of Cetraxal Plus group. The number of patients with adverse reactions was the same for both treatment groups and the intensity of these adverse reactions was, at worse, moderate.

In the second study, Cetraxal Plus was compared to Ciprofloxacin 0.3%; 296 patients under Cetraxal Plus and 294 under Ciprofloxacin 0.3% were included. Cetraxal Plus administered as 4-6 drops t.i.d for 8 days, constitutes an effective treatment against diffuse otitis externa.

Cetraxal Plus was superior to Ciprofloxacin 0.3% alone for the clinical cure and the total symptom score. When the symptoms were studied individually, the efficacy of the combination was superior to Ciprofloxacin alone for ear swelling and discharge from the ear, but not for ear pain. Cetraxal Plus had a good safety profile. The percentage of adverse events was very low.

The studies in otitis media were assessed the efficacy and safety of Ciprofloxacin 0.3% plus Fluocinolone Acetonide 0.025% (CIPRO+ FLUO) otic solution compared with Ciprofloxacin 0.3% (CIPRO) otic solution and with Fluocinolone Acetonide 0.025% (FLUO) otic solution in the treatment of AOMT in paediatric patients treated with one vial of medication b.i.d. for 7 days.

Both studies demonstrated that Cetraxal Plus was superior to CIPRO and to FLUO for the time to cessation of otorrhea in paediatric patients suffering from otitis media. Moreover, Cetraxal Plus and CIPRO were statistically significantly better than FLUO for the sustained microbiological cure (eradication or presumed eradication in the bacteriologic response at both "end of treatment" and "end of study").

VI.2.3 Unknowns relating to treatment benefits

Not applicable.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
UNTREATED INFECTION (BACTERIAL OR FUNGAL OR VIRAL INFECTIONS) DUE TO PATHOGEN RESISTANCE OR CLINICAL SIGNS MASKED FOR THE USE OF CORTICOSTEROIDS	Infection has been observed uncommonly (≥1/1000 to <1/100)	If concomitant skin infections are present or develop, an appropriate antifungal or antibacterial agent should be used. If a favourable response does not occur promptly, use of Cetraxal Plus should be discontinued until the infection has been adequately controlled.
MEDICATION ERROR – Ophthalmic use instead of auricular use	Cetraxal Plus has been administered by ophthalmic route instead of otic route by mistake.	The correct route of administration (auricular) is clearly mentioned in the text of SmPC, PIL and carton box.

Important potential risks

Risk	What is known	Preventability
HYPOTHALAMIC-PITUITARY-ADRENAL AXIS SUPPRESSION	It is a class effect Reversible hypothalamic-pituitary-adrenal (HPA) axis suppression has to do with suppression of the body energy reserves, ability to handle stress, regulating hormonal and nervous system activity as well as modulating immune function). It has occurred in some patients receiving topical corticosteroid at total doses higher than 2 g. However, no HPA axis suppression has been described after otically administered corticosteroids. Considering the low total dose after a treatment with Cetraxal Plus, it is unlikely that the systemic exposure of this drug could lead to measurable changes in cortisol levels.	If HPA axis suppression is noted (your body will not be able to properly regulate your stress and energy levels, which can manifest in fatigue, suppressed immune system, depression, and anxiety), an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid. Recovery of HPA axis function is generally prompt upon discontinuation of topical corticosteroids. Infrequently, signs and symptoms of glucocorticosteroid insufficiency may occur requiring supplemental systemic corticosteroids.

Missing information

Risk	What is known	Preventability
USE IN CHILDREN <6 MONTHS	Safety and efficacy of Cetraxal Plus have not been established in children younger than 6 months. Under exceptional circumstances, Cetraxal Plus treatment could be used in this sub-paediatric population after a very careful benefit/risk evaluation by the prescribing physician taking into account that although there are no known safety concerns or differences in disease process to preclude use in these children, clinical experience is insufficient in this specific subgroup of paediatric population.	In the Posology section it is mentioned that Cetraxal Plus is indicated for children aged 6 months and older. A warning in section 4.4 is included to prevent the use of Cetraxal Plus in this population.

VI.2.5 Summary of risk minimisation measures by safety concern

Not applicable.
No additional risk minimisation measures by safety concern are planned.

VI.2.6 Planned post authorisation development plan

Not applicable.
No post-authorisation studies are currently planned.

VI.2.7 Summary of changes to the Risk Management Plan over time

No changes to the risk management plan over time are anticipated.