

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Gentisone HC Ear Drops.

Gentamicin 0.3% w/v and Hydrocortisone acetate 1% w/v Ear Drops

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

This medicine is a sterile aqueous suspension in 10 ml dropper bottles containing gentamicin sulfate, equivalent to 0.3% w/v gentamicin base and 1.0% w/v hydrocortisone acetate.

Excipients with known effect:

Benzalkonium chloride 50% w/v solution (0.02% w/v per 10ml)

3 PHARMACEUTICAL FORM

Sterile, isotonic solution in dropper bottles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicine is indicated in adults and children:

1. For the treatment of eczema and infection of the outer ear (otitis externa).
2. For prophylaxis against otitis externa following trauma.
3. For post-operative local use in surgery to infected mastoid cavities.

4.2 Posology and method of administration

Posology

Adults, the elderly and the paediatric population

The area should be cleaned and 2 - 4 drops instilled in the affected ear three to four times a day and at night. Alternatively, wicks medicated with this medicine may be placed in the external ear or mastoid cavity.

Method of administration

Auricular use only.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Myasthenia gravis.

Known or suspected perforation of the ear drum.

4.4 Special warnings and precautions for use

Long-term continuous topical therapy should be avoided. Prolonged use may lead to skin sensitisation and the emergence of resistant organisms. Cross sensitivity with other aminoglycoside antibiotics may occur.

In severe infections, topical use of this medicine should be supplemented with appropriate systemic antibiotic treatment.

The condition of the ear drum must always be checked before this medicinal product is prescribed. The medicinal product must not be used if the integrity of the ear drum cannot be guaranteed.

Gentamicin may cause irreversible partial or total deafness when given systemically or when applied topically to open wounds or damaged skin. This effect is dose-related and is enhanced by renal and/or hepatic impairment and is more likely in the elderly.

Irreversible toxic effects may result from direct contact of gentamicin with the middle and inner ear. The benefits of gentamicin therapy should be considered against the risk of infection itself causing hearing loss.

Serious adverse reactions including neurotoxicity, ototoxicity and nephrotoxicity have occurred in patients receiving systemic gentamicin therapy. Although these effects have not been reported following topical optic use of gentamicin, caution is advised when used concomitantly with systemic aminoglycosides.

There have been observed cases of an increased risk of ototoxicity with aminoglycosides administered to patients with mitochondrial mutations, particularly the m.1555A>G mutation, including cases where the patient's aminoglycoside serum levels were within the recommended range. Some cases were associated with a maternal history of deafness and/or mitochondrial mutation. Mitochondrial mutations are rare, and the penetrance of this observed effect is unknown.

This medicine contains benzalkonium chloride which may irritate the skin.

Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects.

Visual disturbance

Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Paediatric population

In infants there is a theoretical risk that sufficient steroid may be absorbed to cause adrenal suppression.

4.5 Interaction with other medicinal products and other forms of interaction

None relevant to topical use.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety for use in pregnancy has not been established. Topical administration of any corticosteroid to pregnant animals can cause abnormalities of foetal development. This medicine should only be used in pregnancy when considered essential by the physician, after careful assessment of the potential risks and benefits.

Breast-feeding

Safety for use in lactation has not been established. This medicine should only be used in lactation when considered essential by the physician, after careful assessment of the potential risks and benefits.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

In the event of irritation, sensitisation or super-infection, treatment with Gentisone HC Ear drops should be discontinued and appropriate therapy instituted. The undesirable effects listed below have been reported at the following frequency:

Not known (cannot be estimated from available data)

System organ class	Frequency	Undesirable effects
Ear and labyrinth disorders	Not known	- Local sensitivity - Ototoxicity - Vestibular disorder: - Hearing loss
Skin and subcutaneous tissue disorders	Not known	- Burning sensation - Stinging - Itching (pruritus): - Dermatitis.
Eye disorders	Not known	- Vision blurred (see also section 4.4)

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal

product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose
Not applicable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiinfectives
ATC code: S03AA

Mechanism of action:

Gentamicin is mixture of antibiotic substances produced by the growth of micromonospora purpurea. It is a bactericidal antibiotic which acts by inhibiting protein synthesis. It has greater antibacterial activity than streptomycin, neomycin or kanamycin.

Gentamicin exerts a number of effects on cells of susceptible bacteria. It affects the integrity of the plasma membrane and the metabolism of RNA, but it's most important effect is inhibition of protein synthesis at the level of the 30s ribosomal subunit.

Corticosteroids, such as hydrocortisone acetate, are used in pharmacological doses for their anti-inflammatory and immuno-suppressant glucocorticoid properties which suppress the clinical manifestation of disease in a wide range of disorders.

5.2 Pharmacokinetic properties

Absorption

Topical application of gentamicin can result in some systemic absorption. Treatment of large areas can result in plasma concentrations of up to 1µg/ml.

Hydrocortisone acetate is not absorbed through the skin as rapidly as hydrocortisone and therefore has a prolonged action. Some is absorbed systemically, where greater than 90% is protein bound.

Distribution

Gentamicin is 70-85% bound to plasma albumin following administration.

Effective plasma concentration is 4 - 8ug/ml
The volume of distribution (V_D) is 0.3 l/kg

Biotransformation

> 70% hydrocortisone acetate is metabolised by the liver.

Elimination

> 90% Gentamicin is excreted unchanged in the urine by glomerular filtration.

$T_{1/2}$ = 2 - 3 hours in individuals with normal kidney function, but can be increased in cases of renal insufficiency.

The elimination rate constant is;

0.02 Hr⁻¹ for anuric patients*

0.30 Hr⁻¹ normal

*Therefore in those with anuria care must be exercised.

The metabolites are excreted in the urine.

Plasma $T_{1/2}$ = 1½ hours.

5.3 Preclinical safety data

See section 4.6

6.1 List of excipients

Benzalkonium chloride (preservative), povidone, polyethylene glycol 4000, sodium chloride, borax, disodium edetate and Water for Injections.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years. Discard contents 4 weeks after opening.

6.4 Special precautions for storage

Store below 25°C. Do not freeze or mix with other liquids.

6.5 Nature and contents of container

10ml dropper bottles.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

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8 **MARKETING AUTHORISATION NUMBER(S)**
PL 20072/0058

9 **DATE OF FIRST AUTHORISATION/RENEWAL OF THE
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28/10/2024

10 **DATE OF REVISION OF THE TEXT**

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