SUMMARY OF PRODUCT CHARACTERISTICS

NAME OF THE MEDICINAL PRODUCT

AURICULARUM, powder and solvent for suspension for ear instillation

QUALITATIVE AND QUANTITATIVE COMPOSITION

Oxytetracycline hydrochloride ..... 100.0 mg
Polymyxin B sulphate ..... 12.3 mg
Dexamethasone sodium phosphate ..... 10.0 mg
Nystatin ..... 1,000,000 IU
Per bottle

Excipient(s) with known effect: Sodium Lauryl Sulphate

For the full list of excipients, see section" List of excipients".

PHARMACEUTICAL FORM

Powder and solvent for suspension for ear instillation.

CLINICAL PARTICULARS

Therapeutic indications

Local treatment:

- of external otitis of bacterial and/or fungal origin;
- chronic otitis:
  - pre-operatively to dry out,
  - post-operatively for petromastoid radical cavities with or without tympanoplasty.

Take into account the official recommendations relating to the appropriate use of antibiotics.

Posology and method of administration

Auricular local route.

Posology

In powder form:
Insufflate a dose of the product obtained by pressing the bottle into the ear canal of the affected ear 1 to 2 times a day, or every 2 to 3 days.

In suspension form:
From the suspension thus obtained, instill 5 to 10 drops into the auditory canal of the affected ear once or twice daily.

Method of administration

In powder form:
Hold the flexible bottle head down; pack all of the powder into the neck;
Press the bottle to obtaine a dose of product.

In suspension form:
In certain particular cases, it is possible to use the suspended powder in the contents of the ampoule of solvent.
This auricular suspension prepared at the time of use retains its activity for 8 days **at between +2°C and +8°C (in the refrigerator).**

Warm the bottle at the time of use by holding it in the palm of the hand for several minutes in order to prevent the unpleasant contact of the cold solution with the ear. Shake vigorously before use.
With the head tilted, instill the drops into the affected ear pulling the outer ear several times. Keep the head tilted to one side for about 5 minutes to promote the penetration of the drops into the external auditory canal. If necessary, repeat for the other ear.
At the end of treatment, the remainder of the bottle must be discarded and must not be retained for reuse.

Treatment duration:
The treatment duration is usually 7 days and may be up to 15 days at most in the treatment of otomycosis.

Contra-indications

Hypersensitivity to the active substances or another product of the cyclin series, or to any of the excipients listed in section “List of excipients”.

Dry perforation of the eardrum (see section “Special warnings and precautions for use”),
Viral infections of the external auditory canal, including varicella and *Herpes simplex* infections.

Special warnings and precautions for use

Check the state of the eardrum before any prescription.
This product contains oxytetracycline, a cycline antibiotic, which, after administration by the systemic route, is known for its toxicity to the teeth of children aged less than 8 years and for the risk of photosensitisation.
In the absence of data on the medicine administered in auricular powder or suspension form, these risks cannot be totally ruled out but are undoubtedly minimal given the quantity administered; the penetration of oxytetracycline into the systemic circulation is even more unlikely when the medicinal product is administered in powder form.
Local administration of antibiotics contributes to sensitisation to the active substances with, potentially, systemic reactions.
The presence of a corticosteroid does not prevent the manifestations of allergy to the antibiotic, but may modify their clinical presentation.
Discontinue treatment as of the first signs of emergence of skin rash or any other sign of local or systemic hypersensitivity.
The attention of sportsmen is drawn to the fact that this product contains an active substance (dexamethasone) which may lead to a positive reaction in tests carried out in the context of anti-doping controls.
The persistence of a deposit of brownish powder in the external auditory canal may necessitate cleaning.
Special attention is to be paid to patients with a hearing aid; indeed, the persistence of the deposit may interfere with hearing-aid operation.
Do not inject, do not swallow.
At the time of use, avoid contact between the nozzle and the ear or fingers in order to limit the risks of contamination.
It is advisable to not combine this medicine with another local treatment.
If, after 10 days, or after 15 days in the event of otomycosis, symptoms persist, the patient is to return for reevaluation of the disease and treatment.

This medicine contains 3.25 mg sodium laurilsulfate in each bottle.
Sodium laurilsulfate may cause local skin reactions (such as stinging or burning sensation) or increase skin reactions caused by other products when applied on the same area.

Fertility, pregnancy and lactation

Pregnancy
This medicine is only to be used during pregnancy if necessary.

Lactation
This medicine may be prescribed during breast-feeding.

Undesirable effects

- Exceptionally: hot sensation or itching at the start of treatment, local allergy, dizziness.
- Persistence of brownish residues in the auditory canal (see section “Special warnings and precautions for use”).
- Selection of resistant microorganisms.

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 national reporting system: Agence nationale de sécurité du medicament et des produits de santé (ANSM) and network of the Regional Centres of Pharmacovigilance – Website: www.signalement-sante.gouv.fr

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmacotherapeutic group: otologicals; corticosteroid and anti-infectives in combination; dexamethasone and anti-infectives. ATC code: S02CA06.

Dexamethasone is a steroidal anti-inflammatory.
Oxytetracycline is an antibiotic in the cycline series.
Polymyxin B is an antibiotic in the polypeptide series.
Nystatin is an antifungal.
Antibiotic, antifungal and anti-inflammatory activity in otology due to the anti-inflammatory properties of dexamethasone, antifungal action of nystatin and antibacterial action of the two antibiotics with complementary activity.
The combination of the two antibiotics is justified by their good local tolerability and by the microorganisms encountered in middle-ear infections. Moreover, the combination of oxytetracycline and polymyxin B is synergistic. This property allows to widen the spectrum to include *Pseudomonas* and all *Proteus*.

ANTIBACTERIAL ACTIVITY SPECTRUM OF OXYTETRACYCLINE AND POLYMYXIN B.

OXYTETRACYCLINE

The critical concentrations separate sensitive strains from strains with intermediate sensitivity and the latter from resistant strains:

S $\leq$ 4 mg/l and R > 8 mg/l

The prevalence of acquired resistance may vary as a function of geography and time for certain species.
It is thus of value to have information on the prevalence of local resistance, particularly for the treatment of severe infections. These data can only orient the probability of sensitivity of a bacterial strain to the antibiotic.
When the variability of the prevalence of resistance in France is known for a given bacterial species, it is shown in the following table:

Category	Frequency of acquired resistance in France (>10%) (range)
SENSITIVE SPECIES	
Gram-positive aerobes	
Bacillus	40-80%
Enterococcus	
Methicillin-sensitive *Staphylococcus* *	70-80%
Methicillin-resistant *Staphylococcus* **	20%
Streptococcus A	80-90%
Streptococcus B	20-40%
Streptococcus pneumoniae	
Gram-negative aerobes	
Branhamella catarrhalis	20-40%
Brucella	10%
Escherichia coli	10-30%
Haemophilus influenzae	
Klebsiella	
Neisseria gonorrhoeae	
Pasteurella	
Vibrio cholerae	
Anaerobes	
Propionibacterium acnes	
Category	**Frequency of acquired resistance in France (>10%) (range)**
Other	
Borrelia burgdorferi	
Chlamydia	
Coxiella burnetii	
Leptospira	
Mycoplasma pneumoniae	
Rickettsia	
Treponema pallidum	
Ureaplasma urealyticum	
RESISTANT SPECIES	
Gram-negative aerobes	
Acinetobacter	
Proteus mirabilis	
Proteus vulgaris	
Pseudomonas	
Serratia	

* Clinical efficacy demonstrated for the sensitive strains in the approved clinical indication in combination with polymyxin B.
** The frequency of methicillin-resistance is 30 to 50% for all Staphylococci and is mainly encountered in hospital environments.

POLYMYXIN B

The critical concentrations separate sensitive strains from strains with intermediate sensitivity and the latter from resistant strains:
S ≤ 2 mg/l and R > 2 mg/l

The prevalence of acquired resistance may vary as a function of geography and time for certain species. It is thus of value to have information on the prevalence of local resistance, particularly for the treatment of severe infections. These data can only orient the probability of sensitivity of a bacterial strain to the antibiotic.

When the variability of the prevalence of resistance in France is known for a given bacterial species, it is shown in the following table:

Category	Frequency of acquired resistance in France (>10%) (range)
SENSITIVE SPECIES **Gram-negative aerobes** *Acinetobacter* *Aeromonas* *Alcaligenes* *Citrobacter freundii* *Citrobacter koseri* *Enterobacter* *Escherichia coli* *Klebsiella* *Moraxella* *Pseudomonas aeruginosa** *Salmonella* *Shigella* *Stenotrophomonas maltophilia*	0-30%
RESISTANT SPECIES **Gram-positive aerobes** Cocci and bacilli **Gram-negative aerobes** *Branhamella catarrhalis* *Brucella* *Burkholderia cepacia* *Burkholderia pseudomallei* *Campylobacter* *Chryseobacterium meningosepticum* *Legionella* *Morganella* *Neisseria* *Proteus* *Providencia* *Serratia* *Vibrio cholerae El Tor* **Anaerobes** Cocci and bacilli **Other** *Mycobacterium*	

* Clinical efficacy demonstrated for the sensitive strains in the approved clinical indication in combination with oxytetracycline.

Note: the spectrum is for the systemic form of the antibiotics belonging to the polypeptides series. With local pharmaceutical presentations, the concentrations obtained *in situ* are markedly greater than the plasma concentrations. Some uncertainty persists with regard to concentration kinetics *in situ,* the local physicochemical conditions which may modify antibiotic activity and the stability of the product *in situ*.

NYSTATIN

Contact antifungal of the polyene series, extracted from *Streptomyces noursei* culture.
Nystatin would act by binding to the sterol fraction of the fungal membrane, inducing changes in membrane permeability.
Antifungal action spectrum: nystatin is active on a wide variety of yeasts and filamentous fungi, including the main causal agents for otomycosis (*Candida, Aspergillus*)

Pharmacokinetic properties:
In the event of a perforated eardrum, there is no systemic absorption.

PHARMACEUTICAL PARTICULARS

List of excipients
Sodium laurylsulphate
Solvent composition: sodium chloride, purified water.

Shelf life

Before reconstitution: 2 years.
After reconstitution: the suspension for ear instillation may be stored for at most 8 days.

Special precautions for storage

Before reconstitution: store at a temperature not exceeding +25°C.
After reconstitution: the suspension for ear instillation is to be stored at between +2°C and +8°C (in the refrigerator).

Nature and contents of container:

Bottle (PE) of powder and 10 ml of solvent in an ampoule (LDPE); box of 1.

Special precautions for disposal and other handling:
Any unused medicinal product or waste material should be disposed of in accordance with local requirement.

MARKETING AUTHORISATION HOLDER:
Laboratoires GRIMBERG SA – 44 avenue Georges Pompidou- 92300 Levallois-Perret - France

MARKETING AUTHORISATION NUMBER(S)

34009 301 922 5 2: 1 bottle (polyethylene) – 1 ampoule of 10 ml (low density polyethylene)
34009 364 014 8 8: 1 bottle (polyethylene) – 1 ampoule of 10 ml (low density polyethylene)

DATE OF FIRST AUTHORISATION / RENEWAL OF AUTHORISATION
06 August 1987/06 August 2012

DATE OF REVISION OF THE TEXT:
03 september 2020

PRESCRIBING AND DISPENSING CONDITIONS

Medicinal product subject to medical prescription.