SUMMARY OF PRODUCT CHARACTERISTICS

LIKACIN 5% Gel

1. NAME OF THE MEDICINAL PRODUCT

LIKACIN 5% Gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

100 g of gel contain:

Active principle:

Amikacin sulfate equivalent to Amikacin 5.0 g

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gel for cutaneous use.

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

Short-term treatment of serious infections caused by susceptible Gram-negative bacteria.

4.2. Posology and method of administration

Apply gel on skin once a day (3-5 cm or more, according to the size of the area to be treated) and rub gently.

4.3. Contraindications

Known individual hypersensitivity to amikacin and to other aminoglycosides.

4.4. Special warnings and precautions for use

Amikacin is potentially nephrotoxic, ototoxic and neurotoxic. To prevent accumulation phenomena, do not use Amikacin with other ototoxic or nephrotoxic agents.

Ototoxicity: in patients suffering from renal insufficiency, for whom treatment is prescribed for more than 5 days, it is advisable to carry out an audiogram before therapy as well as in the course of treatment. In case tinnitus, hearing impairment or a decrease in high-frequency perception is observed, treatment should be suspended.

Nephrotoxicity: since therapy with Amikacin can cause alterations of the renal function, creatinine blood levels should be regularly checked during therapy. To reduce irritation of the renal tubules, the patient should be properly hydrated, since Amikacin is found in urine at high concentrations. If any signs of renal insufficiency are observed, hydration should be consequently increased. In addition, a change in posology should be taken into consideration. In case of increased azotemia or progressive diuresis reduction, treatment should be suspended.
Neurotoxicity: since Amikacin at high doses has caused muscle paralysis in lab animals, the possibility of neuromuscular block and respiratory paralysis should be reckoned with, whenever Amikacin is administered with anesthetics or neuromuscular α blockers. If neuromuscular block does occur, administration of calcium salts can neutralize the symptom. Cross-allergy phenomena with other aminoglycosides are possible. As in the case of other antibiotics, therapy with Amikacin can lead to super-infections caused by other resistant germs. In this case, therapy should be immediately suspended and replaced by proper treatment. Use of topical products, especially for prolonged periods, may lead to sensitization. Due to its methyl-p-hydroxybenzoate and propyl-p-hydroxybenzoate content, the product may cause urticaria; delayed-type reactions (contact dermatitis) occur more frequently, whereas immediate reactions such as urticaria and bronchospasm are observed more rarely.

Keep out of sight and reach of children

4.5. Interaction with other medicinal products and other forms of interaction

Do not administer the preparation together with rapid-action diuretics such as ethacrynic acid, furosemide and mannitol, due to the possibility of rapid hear loss. Associations with other aminoglycosides, cefaloridin, colistin and paromomycin can increase the risk of renal and otovestibular damage.

4.6. Pregnancy and lactation

Pregnant women and infants should be treated with Amikacin only if absolutely necessary and under direct medical supervision. It is unknown whether Amikacin is excreted with human milk. Therefore, as a rule, in such cases the product should better not be given or nursing suspended.

4.7. Effects on ability to drive and use machines

The preparation does not interfere with driving ability or with the use of machines.

4.8. Undesirable effects

The main therapy-related adverse reactions caused by Amikacin, usually associated to higher doses or longer administration periods than recommended, are: toxicity localized at the VIIIth pair of cranial nerves (especially ototoxicity) accompanied by tinnitus, dizziness, partial deafness and nephrotoxicity with albuminuria, presence of leukocytes, erythrocytes and cylindroids in the sediment, hyperazotemia and oliguria. In addition to the above mentioned side effects there have been also cases of hypersensitivity-related cutaneous rash, iatrogenic fever, cephalea, paresthesia, tremors, nausea and vomit, eosinophilia, anemia, hypotension.

4.9. Overdose

There have been no known cases of overdose with Amikacin for topical use.

5. PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmacotherapeutic category: antibiotics for dermatological use
Amikacin is a semisynthetic antibiotic of the aminoglycoside family. Its bactericidal action mechanism is similar to that of all other aminoglycosides and consists of the inhibition of protein synthesis by the microorganism, due to the creation of a highly stable bond between the antibiotic and ribosomal aggregation site. In vitro Amikacin has a broad spectrum of action including several gram-positive and gram-negative microorganisms: Staphylococcus aureus (including penicillinase-producing and methicillin-resistant strains), E.Coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, positive and negative Proteus indole, Providentia stuartii, Salmonella s.p.p., Shigella s.p.p., Acinetobacter.

Amikacin is not degradable by most enzymes that inactivate other aminoglycosides. Therefore, all microorganisms that are resistant against gentamicin, tobramycin and kanamycin are sensitive towards Amikacin.

5.2. Pharmacokinetic properties

Kinetic studies have shown that maximum serum peak (22.8 mcg/mL) following administration of 7.5 mg/kg/i.m., occurs after 30-60', while drug plasmatic half-life in subjects with a normal renal function, is about 2-3 hours. Therapeutically useful blood levels of the drug have been observed up to 10 -12 hours following administration. Following slow i.v. infusion (7.5 mg/kg in 1-2 h), Amikacin blood levels at the end of the infusion amount to 37.5 mcg/mL with a half-life of about 2 hours. The drug is not metabolized by the organism and its elimination takes place through the kidney (over 90% of the administered dose is excreted with urine within 24 hours). Amikacin bonds to serum proteins for less than 10%. Amikacin readily spreads through the organism tissues and fluids, such as the peritoneal cavity, pleural fluid and bronchial secretions, reaching therapeutically useful levels ranging between 10-20% of serum levels. An amount of Amikacin corresponding to 10-20% of the serum levels spreads through intact meningitides, reaching a 50% level in case of meningitis. Amikacin can pass through the placental barrier and is found in fetal blood and amniotic fluid at significant concentrations.

5.3. Preclinical safety data

LD$_{50}$ in mice was 704 mg/kg/i.m.

Subacute toxicity tests in dogs have shown that the drug is well tolerated. No drug-related death occurred (50 mg/kg/i.m.). Chronic toxicity tests in rats have not evidenced any drug-related toxic symptoms (150 mg/kg/i.m.).

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

100 g of gel contain the following excipients:

Hydroxyethyl cellulose, Methyl-p-hydroxybenzoate, Propyl-p-hydroxybenzoate, Glycerin, Purified water.

6.2. Incompatibilities

Not applicable.
6.3. **Shelf-life**

36 months. The indicated shelf-life refers to the product correctly stored in its integral package.

6.4. **Special precautions for storage**

Do not store at temperatures over 30°C

6.5. **Nature and contents of container**

Box containing one 30 g gel tube for cutaneous use.

6.6. **Instructions for use and handling**

As described in the “Posology and Method of Administration” section

7. **MARKETING AUTHORIZATION HOLDER**

Laboratorio Italiano Biochimico Farmaceutico LISAPHARMA S.p.A.
Via Licinio, 11 – 22036 ERBA (CO)

8. **MARKETING AUTHORIZATION NUMBER**

A.I.C. n. 024475081

9. **DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORIZATION**

June 2010

10. **DATE OF REVISION OF THE TEXT**

June 2010