1. NAME OF THE MEDICINAL PRODUCT

Heparin eye drops 500,000 I.U./100 ml eye drops, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

100 ml of Heparin eye drops contain 500,000 I.U. of heparin sodium.
Excipients with known effects
Phosphate buffer 3.80 mg/ml
Multi-dose bottle
Methyl p-Hydroxybenzoate
Propyl p-Hydroxybenzoate
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Eye drops, solution.

4. CLINICAL INFORMATION

4.1 Therapeutic indications
Heparin eye drops are indicated in thermal and chemical burns of the conjunctiva. This medicine is
It is also indicated in all diseases of the anterior part of the eye in which it can be useful
the use of a medicinal product with local fibrinolytic action.

4.2 Dosage and method of administration
Thermal and chemical burns of the conjunctiva
After total elimination of corrosive products by washing and neutralization, instill one drop
of eye drops every hour and for 48 hours. Subsequently the instillations can be spaced out.
Conditions of the anterior part of the eye in which the use of a specific medicine may be useful
fibrinolytic action 2 drops in the conjunctival sac, 2 or more times a day, according to medical prescription.

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients listed in paragraph 6.1.

4.4 Special warnings and precautions for use
Eye drops, solution in multi-dose bottle
This product contains parahydroxybenzoates, as preservatives, which may cause reactions allergic (even delayed)
Eye drops, solution in single-dose containers
This product does not contain preservatives with antimicrobial action to protect it from pollution
occasionally during use. The product must be used for a single dressing and a single
patient and the single-dose container must be discarded even if not completely used.

4.5 Interactions with other medicinal products and other forms of interaction
There are no known interactions.

4.6 Fertility, pregnancy and breastfeeding
Pregnancy
No clinical data are available on the safety of use of Heparin eye drops in pregnant women.
Heparin eye drops should be administered during pregnancy only if clearly indicated.

Breastfeeding
No clinical data are available on the safety of using Heparin eye drops during breastfeeding.
Heparin eye drops should not be used during breastfeeding.

4.7 Effects on the ability to drive and use machines
Heparin eye drops have no or negligible influence on the ability to drive or use vehicles
machinery.

4.8 Undesirable effects
With local ophthalmic use, no systemic side effects related to the drug are to be expected administration of heparin by other routes (intramuscular, intravenous, oral), also due to the very modest dosages with which the substance is used locally. Given the presence of phosphates, a lot rarely have cases of corneal calcification associated with the use of eye drops containing phosphates in patients with significantly damaged cornea.
Reporting of suspected adverse reactions
Reporting of suspected adverse reactions that occur after authorization of the medicinal product is important, as it allows continuous monitoring of the benefit/risk ratio of the medicinal. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system at https://www.aifa.gov.it/content/segnalazioni-reazioniavverse.

4.9 Overdose
No symptoms of overdose have been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Other ophthalmics; heparin: ATC code: S01XA14
Mechanism of action
Heparin is an acidic, sulphonated mucopolysaccharide, provided with direct anticoagulant activity and immediate both in vitro and in vivo.
The anticoagulant activity of heparin is the result of its high affinity for antithrombin III.
The interaction induces a conformational change of ATIII and confers activity on the complex as a potent inhibitor of coagulation factors such as factor II (thrombin) and Xa. Furthermore the factors IXa, XIa and XIIa are inhibited by the ATIII-heparin complex.
Among the biological activities of heparin, the anti-inflammatory effects resulting from it should be remembered inhibition of activated granulocytes, inhibition that prevents the release of free radicals, proteases and others chemical mediators of inflammation.
Heparin also has a profibrinolytic effect through the stimulation and release of tPA.
The characteristic of promoting the reabsorption of exudates at the conjunctival level and the lysis of material protein in the anterior chamber of the eye (for a probable indirect activity) is the one that comes most used in ophthalmology.
Subconjunctival injection in rabbits (and humans) produces improvement in anterior uveitis and a decrease in intraocular tone.

5.2 Pharmacokinetic properties
For systemic administration, heparin is rapidly taken up by endothelial cells and therein presents rates higher than those in plasma. It binds strongly to plasma proteins. It is demoted to oligosaccharides which are then excreted in the urine.
The topical application of heparin in rabbits by ocular instillation has shown that, for example intact eye, it does not pass into the anterior chamber when its concentration is 5%. Only at concentration of 30% it is found in the aqueous humor, but this concentration produces a partial damage to the corneal epithelium detectable only with fluorescein.
In experimental lesions caused by thermal or chemical agents, 5% heparin causes marked regression of hyperemia, edema and ulcerations.

5.3 Preclinical safety data
Preclinical data reveal no special risks for humans based on conventional safety studies pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity of reproduction and development.

6. PHARMACEUTICAL INFORMATION

6.1 List of excipients
Eye drops, solution - multidose bottle
Dibasic sodium phosphate, monobasic sodium phosphate, sodium chloride, sodium edetate, p-Hydroxybenzoate of methyl, propyl p-Hydroxybenzoate and water for injections.

Eye drops, solution - single-dose containers
Dibasic sodium phosphate, dihydrogen sodium phosphate, sodium chloride, sodium edetate and water for injectable preparations.

6.2 Incompatibilities
There are no known incompatibilities with other medicines.

6.3 Validity period
Eye drops, solution - multidose bottle: 30 months
This product should not be used more than 30 days after first opening the container.
Once the term has elapsed, any remaining eye drops must be discarded.
Eye drops, solution - single-dose containers: 3 years

The single-dose container does not contain preservatives, therefore this product should be used immediately afterwards the opening of the container which must be eliminated even if only partially used. After opening the aluminum pouch, the single-dose containers must be used within three months; after this deadline, residual containers must be eliminated.

6.4 Special precautions for storage
No particular precautions.

6.5 Nature and contents of the container
Multi-dose bottle
Polyethylene dropper bottle containing 5 ml of eye drops.

Single-dose containers
Box of 10 single-dose containers of 0.5 ml enclosed in strips of 5 containers in PE-Al bags.

6.6 Special precautions for disposal and handling
No special disposal instructions.
Unused medicine and waste products from that medicine must be disposed of accordingly to current local legislation.

Handling
Multi-dose bottle
No particular instructions.

Single-dose container
Remove a single-dose container from the bag and shake it before opening it, to homogenize it solution contained therein.

Open the single-dose container by detaching the cap above the dropper spout.
Using moderate pressure on the body of the container, allow the liquid to drip into the conjunctival sac medicine in the desired quantity.
In case of administration by subconjunctival or retrobulbar injection, the withdrawal of the medicine using a syringe equipped with a needle is facilitated by preventive removal by cutting with scissors sterilized, with

the dropper nozzle.

7. MARKETING AUTHORIZATION HOLDER

Farmigea S.p.A. - Via G.B. Oliva 6/8, 56121 – Pisa
Sales dealer: POLIFARMA S.p.A. Viale dell'Arte 69, 00144 Rome

8. MARKETING AUTHORIZATION NUMBERS

Heparin Eye Drops 500,000 U.I./100 ml eye drops, solution - 5 ml bottle - A.I.C. 009956018
Heparin Eye Drops 500,000 I.U./100 ml eye drops, solution - 10 single-dose containers of 0.5 ml – AIC 009956020

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORIZATION

22 April 1955 /1 June 2010