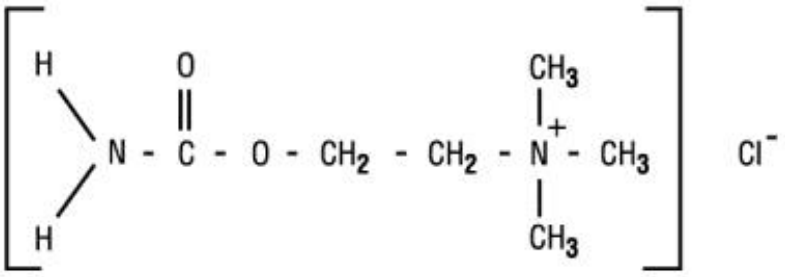
## 1. NAME OF THE MEDICINAL PRODUCT
MIOSTAT 0.01% Intraocular Solution

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION
MIOSTAT (carbachol intraocular solution, USP) is a sterile balanced salt solution of carbachol for intraocular injection. The active ingredient is represented by the chemical structure:



Established name: Carbachol
Chemical name: Ethanaminium, 2-[(aminocarbonyl) oxy]-N,N,N-trimethyl-, chloride.
Molecular Formula: $C_6H_{15}ClN_2O_2$
Molecular Weight: 182.65

**Active**: 1 ml solution contains 0.1 mg carbachol.
For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM
Solution for injection, intraocular use.

## 4. CLINICAL PARTICULARS
### 4.1. Therapeutic Indications
Intraocular use for obtaining miosis during surgery. In addition, MIOSTAT (carbachol intraocular solution, USP) reduces the intensity of intraocular pressure elevation in the first 24 hours after cataract surgery.

### 4.2. Posology and Method of Administration
**Posology**
Instillation into the anterior chamber for the production of miosis by injection; for single dose intraocular only.

**Method of Administration**
Use in adults, including elderly
Perform the operations listed below under aseptic conditions:
1. Peel the backing paper from the blister package and drop the bottle of MIOSTAT onto a sterile tray.
2. Remove a sterile disposable syringe from the protective packaging.
3. Place a 21 gauge bevelled needle securely on the end of the syringe with a twisting motion.
4. Draw 1.5 ml of air into the syringe with the needle protector still in place.
5. While holding the MIOSTAT Solution vial firmly, remove the needle protector and introduce the 21 gauge needle into the vial.

6. Inject the air into the vial and withdraw the solution into the syringe.
7. After MIOSTAT has been completely transferred to the syringe, withdraw the needle from the vial and remove the needle from the syringe.
8. After securely placing a 27-gauge blunt tip cannula on the syringe, the product is ready for injection.

No more than one-half millilitre (0.5 mL) should be instilled into the anterior chamber for the production of satisfactory miosis. It may be instilled before or after securing sutures. Miosis is usually maximal within 2 to 5 minutes after application.

### 4.3. Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients.

### 4.4. Special Warnings and Precautions for Use

- MIOSTAT should be used with caution in patients with acute cardiac failure, bronchial asthma, peptic ulcer, hyperthyroidism, G.I. spasm, urinary tract obstruction and Parkinson's disease.
- The use of MIOSTAT may increase surgically induced intraocular inflammation.
- The vial stopper contains natural rubber (latex) which may cause severe allergic reactions.

### 4.5. Interaction with other Medicinal Products and Other Forms of Interaction

No clinically relevant interactions have been described.

### 4.6. Pregnancy and Lactation

Fertility

Studies have not been performed to evaluate the effect of topical ocular administration of carbachol on human fertility.

**Pregnancy**

There are no or limited amount of data from the use of carbachol in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. MIOSTAT should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Breastfeeding**

It is unknown whether carbachol is excreted in human milk. There is also no information on the safety of carbachol ophthalmic formulations used during breastfeeding. However, a risk to the suckling child cannot be excluded.

### 4.7. Effects on Ability to Drive and Use Machines

Miosis may cause blurred vision and difficulty in dark adaptation. If temporary blurred vision occurs following surgery where MIOSTAT was used, the patient must wait until vision clears before driving or using machinery.

### 4.8. Undesirable Effects

The following adverse reactions have been reported during clinical trials with carbachol intraocular solution and are classified according to the subsequent convention: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000) and very rare (<1/10,000). Within each frequency-grouping, adverse reactions are presented in order of decreasing seriousness.

| System organ classification | Adverse reactions<br>[MedDRA Preferred Term (v.24.1)] |
|---|---|
| Nervous system disorders | Uncommon: headache |
| Eye disorders | Uncommon: intraocular pressure increased |

Additional adverse reactions identified from post-marketing surveillance include the following. Frequencies cannot be estimated from the available data.

| System organ classification | Adverse reactions<br>[MedDRA Preferred Term (v.15.1)] |
|---|---|
| Eye disorders | visual impairment, corneal degeneration, corneal opacity, anterior chamber inflammation, corneal oedema, eye inflammation, drug effect prolonged (miosis), vision blurred, eye pain, ocular hyperaemia, persistent bullous keratopathy, retinal detachment and postoperative iritis following cataract extraction. |
| Gastrointestinal disorders | vomiting |

Systemic: Side effects such as flushing, sweating, epigastric distress, abdominal cramps, tightness in urinary bladder and headache have been reported with topical or systemic application of carbachol.

### 4.9. Overdose

In case of overdose, symptoms of toxicity may include: headache, salivation, syncope, bradycardia, hypotension, abdominal cramps, vomiting, asthma and diarrhea. Treatment of overdose is supportive. In cases of severe systemic toxicity, therapy with anticholinergic may be necessary.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1. Pharmacodynamic Properties

Pharmacotherapeutic group: Antiglaucoma Preparations and Miotics; Parasympathomimetics, ATC code: S01EB02

Mechanism of Action:

Carbachol is a parasympathomimetic agent that induces miosis by cholinergic action on the motor nerve endings of the sphincter muscles in the iris. Potent cholinergic agents produce constriction of the iris and ciliary body resulting in lowering of intraocular pressure. The clinical studies carried out in cataract surgery serve as a model to demonstrate efficacy in other intraocular surgical procedures.

### 5.2. Pharmacokinetic Properties

Plasma levels of carbachol have not been studied following intraocular administration of carbachol to humans, but pharmacokinetic data from animal studies are available. Those

studies demonstrate that intravenously injected carbachol is rapidly eliminated from the plasma. In animals, excretion is mainly through the urine. Carbachol is metabolised to choline in plasma following intravenous administration.

### 5.3. Preclinical Safety Data

The available non-clinical data reveal no special hazard for humans based on studies of ocular toxicity and developmental toxicity.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1. List of Excipients

sodium chloride, potassium chloride, calcium chloride dihydrate, magnesium chloride hexahydrate, sodium acetate trihydrate, sodium citrate dihydrate, sodium hydroxide and/or hydrochloric acid (to adjust pH) and water for injection

### 6.2. Incompatibilities

Not applicable.

### 6.3. Special Precautions for Storage

Store below 30°C. Do not refrigerate. Do not freeze.

### 6.4. Nature and Contents of Container

In a 2.0 mL glass vial with a 1.5 mL fill, grey butyl stopper and aluminum seal packaged twelve to a carton.

**NDC** 0065-0023-15

**Rx ONLY**

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