SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Miostat 100 microgram/ml solution for injection for intraocular use

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml solution contains 100 micrograms carbachol.
One 1.5 ml vial contains 150 micrograms carbachol.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection, intraocular use.
Clear, colourless solution, pH 6.5-7.5.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Miostat is indicated to induce rapid and complete miosis in connection with intraocular surgery. Maximal miosis usually occurs within a few minutes following instillation.

4.2 Posology and method of administration

Posology
A maximum of 0.5 ml Miostat (50 micrograms carbachol) is instilled carefully into the anterior chamber. Miostat has been shown to be effective for up to 24 hours following surgery. Effective miosis has been demonstrated in some patients with as little as 5 micrograms of carbachol.

Paediatric patients
Miostat is not recommended for use in children due to a lack of data on efficacy and safety.

Use in the older population
No dose adjustment is necessary in the older population .

Renal and hepatic impairment
No studies have been performed to evaluate the effects of impaired renal or hepatic function on carbachol elimination. As systemic exposure to carbachol following intraocular instillation in humans is taken to be minimal, no adjustment in dose is considered necessary in patients with renal or hepatic impairment.

Method of administration
Miostat is intended for intraocular administration only.

Aseptically remove the vial from the blister pack by peeling off the backing paper and put the vial on a sterile tray. Draw the contents up into a dry sterile syringe and replace the cannula with an atraumatic cannula prior to intraocular administration. Discard unused portion.

4.3 Contraindications

Hypersensitivity to the active substance or any of the excipients.

4.4 Special warnings and precautions for use

- Intraocular carbachol 100 microgram/ml should be used with caution in patients with acute cardiac failure, bronchial asthma, peptic ulcer, hyperthyroidism, gastrointestinal spasm, urinary tract obstruction and Parkinson's disease.
- Patients with a history of iritis/uveitis.
- Use of Miostat may induce intraocular inflammation (iris hyperaemia) beyond that caused by surgery.
- In the event of hypotonia, further reduction in intraocular pressure should be avoided.
- 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 interaction studies have been performed
Under certain conditions, cholinergic agonists can prolong the effects of depolarizing muscle relaxants, reduce the effects of stabilising muscle relaxants and prolong the negative chronotropic effect of cardiac glycosides.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no or limited amount of data from the use of carbachol in pregnant women. The potential risk is felt to be low, considering the single administration of a low dose administered in the eye. Miostat should only be used in pregnant women where the expected benefit outweighs the potential risk to the foetus.

Breastfeeding
It is unknown whether carbachol/metabolites are excreted in human milk. Caution should be exercised when carbachol is administered to nursing mothers.

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

4.7 Effects on ability to drive and use machines

Miostat has a major influence on the ability to drive and use machines.
Miosis may cause blurred vision and difficulty in dark adaptation. If temporary blurring of vision occurs following surgery where Miostat was used, the patient must wait until vision clears before driving or using machinery.

4.8 Undesirable effects

Tabulated summary of adverse reactions
The following undesirable effects are classified according to the following 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), or very rare (<1/10,000), or not known (frequency cannot be estimated from the available data). Within each frequency group, undesirable effects are presented in decreasing order of seriousness. The adverse reactions were obtained from clinical trials and post- marketing spontaneous reports.

System organ classification	Frequency	Preferred term
Nervous system disorders	Uncommon	headache
Eye disorders	Uncommon Rare Not known	intraocular pressure increased retinal detachment, corneal degeneration (bullous keratopathy), uveitis, iritis corneal opacity, corneal oedema visual impairment, anterior chamber inflammation, drug effect prolonged, (miosis), eye pain, ocular hyperaemia, eye inflammation, and blurred vision
Gastrointestinal disorders	Not known	epigastric discomfort, vomiting and nausea

Description of selected adverse reactions
The following undesirable effects have been observed following topical miotic therapy:

System organ classification	Frequency	Preferred term
Nervous system disorders	Common	headache
Eye disorders	Common Uncommon Rare	ciliary muscle spasm, ciliary hyperaemia, conjunctival hyperaemia, photophobia, blurred vision vascular changes in the iris (vasodilation) retinal detachment
Vascular disorders	Uncommon	flushing
Gastrointestinal disorders	Uncommon	abdominal pain, epigastric discomfort
Skin and subcutaneous tissue disorders	Uncommon	hyperhidrosis
Renal and urinary disorders	Uncommon	urinary urgency

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of benefit/risk balance of the medicinal product. Health care professionals are asked to report any suspected adverse reactions via the national reporting system listed in [To be completed nationally]

4.9 Overdose

In the event of overdose, carbachol may cause the same systemic symptoms as cholinesterase inhibitors: Headache, salivation, syncope, bradycardia, hypotension, cardiac failure, abdominal cramps, vomiting, asthma and diarrhoea. In cases of severe toxicity. Atropine sulphate (1 to 2mg) should be given subcutaneously or intramuscularly to control the muscarinic effects. Repeat the treatment every 2 to 4 hours if necessary. Convulsions can be controlled with a short-acting barbiturate.

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 muscle 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 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

In studies in rabbits, Miostat was injected directly into the vitreous body or into the anterior chamber under simulated surgical conditions and the expected pharmacological effects of a miotic were noted. An increased frequency of iritis was found, but there was no significant ocular or retinal toxicity. Transient vasodilation of the iris was seen, attributable to the cholinergic properties of Miostat, but the treatment caused no increase in inflammatory cells or flare values.
No studies on reproductive toxicity or carcinogenic or mutagenic potential have been performed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride,
Potassium chloride (E508),
Calcium chloride dihydrate (E509),
Magnesium chloride hexahydrate (E511),
Sodium acetate trihydrate (E262),
Sodium citrate (E311),
Sodium hydroxide (E524) and/or hydrochloric acid (E507) (to adjust pH)
Water for injection.

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years.

After opening: The solution should be used immediately.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Type I glass vials. 1.5 ml vial with rubber stopped and aluminium overseal in a PVC/Tyvek blister pack.

Each carton contains 12 vials.

6.6 Special precautions for disposal and other handling

Miostat is intended for single use only. Miostat contains no preservative, and consequently any unused solution must be discarded. Only clear solution free from particles should be used.

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

7. MARKETING AUTHORISATION HOLDER

<To be completed nationally>

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

2019-02-13