AUSTRALIAN PRODUCT INFORMATION – MIOCHOL-E (ACETYLCHOLINE CHLORIDE) POWDER FOR SOLUTION FOR INTRAOCULAR IRRIGATION

1 NAME OF THE MEDICINE

Acetylcholine chloride

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial of powder contains acetylcholine chloride 20 mg as the active ingredient. Miochol-E contains acetylcholine chloride 10 mg/mL upon reconstitution with the 2 mL of diluent in the ampoule.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Powder for solution for irrigation and diluent.

Powder: white solid or powder in clear glass vials.

Diluent: clear colourless solution in glass ampoules.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Miochol-E is used to obtain complete miosis of the iris in seconds after placement of the intraocular lens (IOL) in cataract surgery and in penetrating keratoplasty, iridectomy and other anterior segment surgery where rapid miosis may be required.

4.2 DOSE AND METHOD OF ADMINISTRATION

In most cases 0.5 to 2 mL produces satisfactory miosis.

The syringe containing the reconstituted preparation must be fitted with a suitable irrigation cannula for intraocular irrigation.

The Miochol-E solution is instilled into the anterior chamber before or after securing one or more sutures. Instillation should be gentle and parallel to the iris face and tangential to pupil border.

If there are no mechanical hindrances, the pupil starts to constrict in seconds and the peripheral iris is drawn away from the angle of the anterior chamber. Any anatomical hindrance to miosis,

such as anterior or posterior synechiae, must be released to permit the desired effect of the drug.

The solution should be reconstituted immediately before use since aqueous solutions of acetylcholine are unstable.

Instructions for Use and Handling

Warning: Do not use if blister or peelable backing is damaged or broken. Open under aseptic conditions only, at the time of surgery.

Directions for preparing Miochol-E:

1. Inspect unopened blister to ensure that it is intact. The outer package is not sterile. Peel open blister.

2. Aseptically transfer the ampoule, vial and filter hub to sterile field. Maintain asepsis during preparation of solution. Sterile gloves and gowns should be used.

3. Aseptically attach a sterile 18 to 20 gauge, bevelled needle to the luer tip of a sterile disposable syringe with twisting motion to assure secure fit.

4. Break open the ampoule containing the diluent. The One Point Cut (OPC) ampoule must be opened as follows: hold the bottom part of the ampoule with the thumb pointing to the coloured point; grasp the top of the ampoule with the other hand, positioning the thumb at the coloured point and press back to break at the existing cut under the point.

5. Remove the needle protector and withdraw the diluent from the ampoule into the syringe. Discard ampoule.

6. Remove and discard plastic cap from top of vial.

7. Insert the needle through the centre of the vial stopper.

8. Transfer the diluent from the syringe to the vial.

9. Shake gently to dissolve drug.

10. Slowly withdraw the solution from the vial through the needle into the syringe.

11. Discard needle.

12. Aseptically open filter hub pouch.

13. Aseptically attach filter hub onto luer tip of syringe with a twisting motion to assure secure fit.

14. Aseptically attach a sterile blunt tip irrigation cannula to male luer of filter prior to intraocular irrigation.

15. Discard appropriately after use. Do not reuse the filter hub.

The solution must be mixed just before use, since aqueous solutions of acetylcholine are unstable. Only clear and colourless solutions should be used. To reduce microbiological hazard, use as soon as practicable after reconstitution. If storage is necessary, hold at 2-8°C for not more than 6 hours. Any residual quantities of acetylcholine chloride solution should be discarded after a maximum of 6 hours for stability reasons.

Contains no antimicrobial agent. Product is for single use in one patient only. Discard any residue.

Miochol-E should not be re-sterilised. The filter hub is recommended only for use with Miochol-E. Aspiration through the filter is not recommended. However, if utilised, discard needle and syringe filter to prevent recontamination of fluids during injection.

Do not aspirate and inject through the same filter.

Incompatibilities

Reconstitute the solution only with the supplied diluent.

The filter hub is recommended only for use with Miochol-E.

4.3 CONTRAINDICATIONS

Known hypersensitivity to acetylcholine or to any of the excipients.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

In cataract surgery, use Miochol-E only after placement of the IOL. Miochol-E cannot be re-sterilised. Do not gas sterilise. If the blister or peelable packing is damaged or broken, sterility of the enclosed bottle cannot be assured. Open under aseptic conditions only.

Aqueous solutions of acetylcholine chloride are unstable. Prepare solution immediately before use. Only solutions that are clear and colourless should be used. Unused residual amounts should be discarded.

Use in the elderly

No data available

Paediatric use

Safety and effectiveness in children have not been established.

Effects on laboratory tests

No data available

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

None known

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

It is not known if Miochol-E can affect reproductive capacity.

Use in pregnancy – Pregnancy Category B2

Animal reproduction studies have not been conducted with Miochol-E. It is not known whether Miochol-E can cause foetal harm when administered to a pregnant woman. Miochol-E should be given to pregnant women only if clearly needed.

Use in lactation.

It is not known whether Miochol-E is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Miochol-E is administered to nursing women.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

Adverse events considered possibly related or related to use of intraocular acetylcholine and classified according to incidence are reported below:

Frequency	Ocular	Non-Ocular
Uncommon (≥ 1/1,000 and <1/100)	Corneal oedema, corneal clouding, corneal decompensation	None
Rare (≥ 1/10,000 and <1/1,000)	None	Bradycardia, hypotension, flushing, breathing difficulties, sweating.

4.9 OVERDOSE

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

Systemic toxicity is low because of rapid local breakdown. Symptoms of overdose are likely to be effects resulting from systemic absorption (see Section 4.8 Adverse Effects (Undesirable Effects)). In case of overdose, atropine sulfate (0.5 to 1 mg) should be given intramusculary or

intravenously and should be readily available. Adrenaline (0.1 to 1 mg sc) is also of value in overcoming severe cardiovascular or bronchoconstrictor responses.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Acetylcholine is a naturally occurring neurohormone which mediates nerve impulse transmission at all cholinergic sites involving somatic and autonomic nerves. After release from the nerve ending, acetylcholine is rapidly inactivated by the enzyme acetylcholinesterase by hydrolysis to acetic acid and choline.

Direct application of acetylcholine to the iris will cause rapid miosis of short duration. Topical ocular instillation of acetylcholine to the intact eye causes no discernible responses as cholinesterase destroys the molecule more rapidly than it can penetrate the cornea.

Clinical trials

Clinical studies with Miochol-E have shown it to be clinically and statistically superior to placebo in inducing miosis following cataract surgery when administered at doses of 0.5-2.0mL:

Horizontal Pupil Diameter (mm) for Intention to Treat Subjects (mean ± SD)

	Post IOL	Post Injection +45 secs	Post Injection + 5-10 mins
Miochol-E (n=62) Change from post IOL P value - within treatment	7.4 ± 1.5	5.1 ± 1.5 -2.3 ± 1.2 <0.001	4.6 ± 1.4 -2.8 ± 1.2 <0.001
Placebo (n=31) Change from post IOL P value - within treatment	7.1 ± 1.3	6.8 ± 1.4 -0.3 ± 0.5 0.002	6.3 ± 1.6 -0.8 ± 0.8 <0.001

5.2 PHARMACOKINETIC PROPERTIES

Topical: Not applicable.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

The vial contains mannitol as excipient; the ampoule contains diluent which consists of sodium acetate, magnesium chloride hexahydrate, potassium chloride, calcium chloride dihydrate, water for injections.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C. Do not freeze.

6.5 NATURE AND CONTENTS OF CONTAINER

Miochol-E is presented in a blister pack containing one 2 mL Type 1 glass vial with grey rubber stopper and aluminium flip-off cap and one 2 mL Type 1 glass ampoule.

Miochol-E is supplied in a pack containing 1 or 12* blisters and 1 or 12* filter hubs with 5 micron filter, luer lock, respectively.

*not marketed

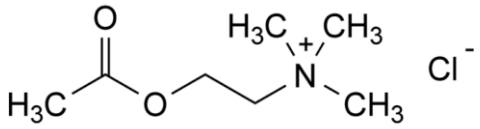
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

Structural formula:



Chemical name: 2-acetoxyethyltrimethylammonium chloride
Molecular formula: $C_7H_{16}ClNO_2$
Molecular weight: 181.7

CAS number

60-31-1

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 – Prescription Only Medicine

8 SPONSOR

Bausch & Lomb (Australia) Pty Ltd

Level 2, 12 Help Street
Chatswood, NSW 2067

9 DATE OF FIRST APPROVAL

16 August 2005

10 DATE OF REVISION

16 September 2020

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	New format
4.2	Remove packaging symbols
6.1	Ingredient names corrected as per international harmonisation of ingredients names