MEMBRANE BLUE - trypan blue injection, solution
Dutch Ophthalmic Research Center (International) B.V.

HIGHLIGHTS OF PRESCRIBING INFORMATION
MembraneBlue™ 0.15% (trypan blue ophthalmic solution). These highlights do not include all the information needed to use MembraneBlue™ 0.15% safely and effectively. See full prescribing information for MembraneBlue™ 0.15%. MembraneBlue™ 0.15% (trypan blue ophthalmic solution) Initial U.S. Approval: 2004

INDICATIONS AND USAGE
For use as an aid in ophthalmic posterior surgery; Facilitating removal of epiretinal tissue.

DOSAGE AND ADMINISTRATION
Prior to injection of MembraneBlue™ 0.15% perform a 'fluid-air exchange'; Carefully apply MembraneBlue™ 0.15% to epiretinal membranes using a blunt cannula; Remove all excess dye; Or Inject MembraneBlue™ 0.15% directly in a BSS filled - vitreous cavity; Wait 30 seconds; Remove all excess dye.

DOSAGE FORMS AND STRENGTHS
MembraneBlue™ 0.15% (trypan blue ophthalmic solution) in a volume of 0.5 mL.

CONTRAINDICATIONS
Insertion of a non-hydrated (dry state), hydrophilic acrylic intraocular lens (IOL).

WARNINGS AND PRECAUTIONS
Excessive staining: Excess MembraneBlue™ 0.15% should be removed from the eye immediately after staining.
Priming of the syringe: make sure the plunger moves smoothly before use: first retract the plunger or twist the plunger in a clockwise motion before injecting the fluid.

ADVERSE REACTIONS
Discoloration of high water content hydrogen intraocular lenses;
Inadvertent staining of the posterior lens capsule and vitreous face;

To report suspected adverse reactions contact Dutch Ophthalmic, USA at 1-800-75-DUTCH or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

USE IN SPECIFIC POPULATIONS
Trypan blue should not be given to pregnant women. (7)

Revised: 11/2009

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**FULL PRESCRIBING INFORMATION**

**MembraneBlue 0.15% - Indications & Usage Section**

MembraneBlue™ 0.15% is indicated for use as an aid in ophthalmic surgery by staining the epiretinal membranes during ophthalmic surgical vitrectomy procedures, facilitating removal of the tissue.

**MembraneBlue 0.15% - Dosage & administration section**

Make sure the plunger moves smoothly before use. Prime the syringe prior to use by retracting the plunger before injecting the fluid. Alternatively, twist the plunger into the stopper in a clockwise motion until tight. Once tight, continue turning the plunger in a clockwise motion until the stopper rotates freely within the syringe, two or three rotations. The syringe is now primed and suitable for injection.

Before injection of MembraneBlue™ 0.15% perform a 'fluid-air exchange', i.e. filling the entire vitreous cavity with air, to prevent aqueous dilution of MembraneBlue™ 0.15%. MembraneBlue™ 0.15% is carefully applied to the retinal membrane using a blunt cannula attached to the MembraneBlue™ 0.15% syringe, without allowing the cannula to contact or damage the retina. Sufficient staining is expected on contact with the membrane. All excess dye should be removed from the vitreous cavity before performing an air-fluid exchange, to prevent unnecessary spreading of the dye.

MembraneBlue™ 0.15% can also be injected directly in a BSS filled vitreous cavity (instead of injecting under air). Clinical use demonstrated that, after complete vitreous and posterior hyaloid removal, sufficient staining is achieved after 30 seconds of application under BSS.

MembraneBlue™ 0.15% is intended to be applied directly on the areas where membranes could be present, staining any portion of the membrane which comes in contact with the dye. The dye does not penetrate the membrane.

**MembraneBlue 0.15% - Dosage forms & strengths section.**

MembraneBlue™ 0.15% (trypan blue ophthalmic solution) is supplied in 2.25 mL syringes filled to a volume of 0.5 mL.

**MembraneBlue 0.15% - Contraindications section.**

MembraneBlue™ 0.15% is contraindicated when a non-hydrated (dry state), hydrophilic acrylic intraocular lens (IOL) is planned to be inserted into the eye. The dye may be absorbed by the IOL and stain it.

**MembraneBlue 0.15% - Warnings and precautions section**

Excessive staining:
It is recommended that after injection all excess MembraneBlue™ 0.15% be immediately removed from the eye.

Priming of the syringe:
Make sure the plunger moves smoothly before use: first retract the plunger or twist the plunger in a clockwise motion before injecting the fluid.

MembraneBlue 0.15% - Adverse reactions section.
Adverse reactions reported following use of MembraneBlue™ 0.15% include discoloration of high water content hydrogen intraocular lenses (see Contraindications) and inadvertent staining of the posterior lens capsule and vitreous face. Staining of the posterior lens capsule or staining of the vitreous face is generally self limited, lasting up to one week.

MembraneBlue 0.15% - Use in specific populations section

MembraneBlue 0.15% - Pregnancy section.
Teratogenic Effects: Pregnancy Category C. Trypan blue is teratogenic in rats, mice, rabbits, hamsters, dogs, guinea pigs, pigs, and chickens. The majority of teratogenicity studies performed involve intravenous, intraperitoneal, or subcutaneous administration in the rat. The teratogenic dose is 50 mg/kg as a single dose or 25 mg/kg/day during embryogenesis in the rat. These doses are approximately 4,000- and 2,000-fold the maximum recommended human dose of 0.75 mg per injection based on a 60 kg person, assuming that the whole dose is completely absorbed. Characteristic anomalies included neural tube, cardiovascular, vertebral, tail, and eye defects. Trypan blue also caused an increase in post-implantation mortality, and decreased fetal weight. In the monkey, trypan blue caused abortions with single or two daily doses of 50 mg/kg between the 20th to 25th days of pregnancy, but no apparent increase in birth defects (approximately 4,000-fold maximum recommended human dose of 0.75 mg per injection, assuming total absorption). There are no adequate and well-controlled studies in pregnant women. Trypan blue should be given to a pregnant woman only if the potential benefit justifies the potential risk to the fetus.

MembraneBlue 0.15% - Nursing mothers section
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when trypan blue is administered to a nursing woman.

MembraneBlue 0.15% - Pediatric use section.
The safety and effectiveness of trypan blue have been established in pediatric patients. use of trypan blue is supported by evidence from an adequate and well-controlled study in pediatric patients.

MembraneBlue 0.15% - Geriatric use.
No overall differences in safety and effectiveness have been observed between elderly and younger patients.

MembraneBlue 0.15% - Description.
MembraneBlue™ 0.15% (trypan blue ophthalmic solution) is a sterile solution of trypan blue (an acid di-azo group dye). MembraneBlue™ 0.15% selectively stains epiretinal membranes during ophthalmic surgical vitrectomy procedures.

Each mL of MembraneBlue™ 0.15% contains: 1.5 mg trypan blue; 1.9 mg sodium mono-hydrogen orthophosphate (Na₂HPO₄•2H₂O); 0.3 mg sodium di-hydrogen orthophosphate (NaH₂PO₄•2H₂O); 8.2 mg sodium chloride (NaCl); and water for injection. The pH is 7.3 - 7.6. The osmolality is 257 - 314
The drug substance trypan blue has the chemical name 3,3’-[3,3’-dimethyl-4,4’-biphenylylene) bis (azo)]
bis (5-amino-4-hydroxy-2,7-naphthalenedisulfonic acid) tetra sodium salt, a molecular weight of 960.8,
a molecular formula of C\textsubscript{34}H\textsubscript{24}N\textsubscript{6}Na\textsubscript{4}O\textsubscript{14}S\textsubscript{4}, and has the following chemical structure:

![Chemical structure of trypan blue](image)

**MembraneBlue 0.15% - Clinical Pharmacology Section.**

**MembraneBlue 0.15% - Mechanism of action section.**

MembraneBlue™ 0.15% selectively stains membranes in the human eye during posterior surgery, such as epiretinal membranes (ERM) and Internal Limiting Membranes (ILM).

**MembraneBlue 0.15% - Nonclinical toxicology section.**

Trypan blue is carcinogenic in rats. Wister/Lewis rats developed lymphomas after receiving subcutaneous injections of 1% trypan blue dosed at 50 mg/kg every other week for 52 weeks (total dose approximately 100,000-fold the maximum recommended human dose of 0.75 mg per injection in a 60 kg person, assuming total absorption).

**MembraneBlue 0.15% - How supplied section.**

MembraneBlue™ 0.15% is supplied as follows:

0.5 mL of MembraneBlue™ 0.15% in a sterile single-use Luer Lok, 2.25 mL glass syringe, grey rubber plunger stopper and tip cap with polypropylene plunger rod in a peel pouch. Five pouched products are packed in one distribution box.

**MembraneBlue 0.15% - Storage and handling section.**

MembraneBlue™ 0.15% is stored at 15 - 25°C (59 - 77°F). Protect from direct sunlight.

*Rx ONLY*

*Manufactured by*

D.O.R.C. international b.v.
Scheijdelveweg 2
3214 VN Zuidland
The Netherlands

*Distributed in the United States by*

Dutch Ophthalmic, USA
10, Continental Drive, Bldg 1
Exeter, NH 03833, USA

Phone: 800-75-DUTCH or 603-778-6929
US Patents 6,696,430 and 6,372,449
MEMBRANEBLUE™ 0.15% (trypan blue ophthalmic solution)

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See package insert for detailed information.

Basic usage instructions:

- Use solution within 1 week from date of opening. Store at 15°C to 25°C (59°F to 77°F). Avoid light.
- For external use only.
- Do not use if solution changes color or becomes cloudy.

For professional use only.

DORC
Dutch Ophthalmic Research Center International BV
Schenkweg 2
The Netherlands

For Dutch:
DORC
Dutch Ophthalmic Research Center International BV
Schenkweg 2
The Netherlands

For US:

US Patent:
6,695,419 and 6,832,449

See package insert for detailed information.

See package insert for detailed information.

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See package insert for detailed information.
### MEMBRANEBLUE

**trypan blue injection, solution**

#### Product Information

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<th>Product Type</th>
<th>Item Code (Source)</th>
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#### Active Ingredient/Active Moiety

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**Inactive Ingredients**

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<tr>
<td>SODIUM PHOSPHATE, MONOBASIC, DIHYDRATE</td>
<td>0.15 mg in 0.5 mL</td>
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<tr>
<td>WATER</td>
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<td>SODIUM PHOSPHATE, DIBASIC, DIHYDRATE</td>
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<td>SODIUM CHLORIDE</td>
<td>4.1 mg in 0.5 mL</td>
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**Packaging**

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<td>5 in 1 CARTON</td>
<td>02/20/2009</td>
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<td>1</td>
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<td>1 in 1 POUCH</td>
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<td>1</td>
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<td>0.5 mL in 1 SYRINGE, GLASS; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)</td>
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**Marketing Information**

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**Labeler** - Dutch Ophthalmic Research Center (International) B.V. (407522184)

**Registrant** - Dutch Ophthalmic Research Center (International) B.V. (407522184)

**Establishment**

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Revised: 12/2018