MEMBRANEBLUE- 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

HIGHLIGHTS OF PRESCRIBING INFORMATION (1)
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 (1)
(1)

- 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. (3)

CONTRAINDICATIONS

Insertion of a non-hydrated (dry state), hydrophilic acrylic intraocular lens (IOL). (4)

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

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

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 aqeous 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 inection 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 absorved. 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.

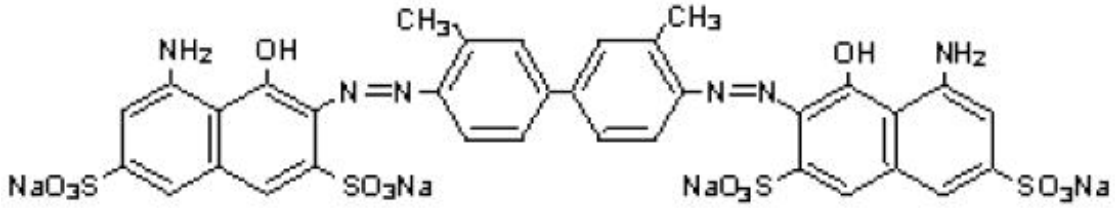
No overall differences in safety and effectiveness have been observed between elderly and younger patients.

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 ($Na_2HPO_4 \cdot 2H_2O$); 0.3 mg sodium di-hydrogen orthophosphate ($NaH_2PO_4 \cdot 2H_2O$); 8.2 mg sodium chloride (NaCl); and water for injection. The pH is 7.3 - 7.6. The osmolality is 257 - 314 mOsm/kg.

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 $C_{34}H_{24}N_6Na_4O_{14}S_4$, and has the following chemical structure:



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% - Package label.Principal display panel

D672e-1

DORC

MEMBRANEBLUE™
0.15%
(trypan blue ophthalmic solution)

DORC DORC DORC *5 SYRINGES* DORC

See package insert for dosing information

Leave syringe in pouch until use. Protect from direct sunlight. Store at 15°C to 25°C (59°F to 77°F). Sterile.

Active ingredients: Trypan blue 0.15%.

Excipient ingredients: Water for injection, Sodium chloride, Sodium phosphate dibasic dihydrate, Sodium phosphate monobasic dihydrate

Labeler code no.: **68803-672** **Rx ONLY**

Dutch Ophthalmic Research Center International BV
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Fax: +31 181 45 80 90
E-mail: mailto@dorc.nl

MEMBRANEBLUE™
0.15%
(trypan blue ophthalmic solution)

Manufactured by
DORC
Dutch Ophthalmic Research Center International BV
Scheijdelveweg 2
3214 VN Zuidland
The Netherlands

Distributed in the USA by
DUTCH OPHTHALMIC USA
Dutch Ophthalmic, USA
10 Continental Drive, Bldg 1
Exeter, NH 03833, USA
Phone: 800-75-DUTCH or 603-778-6929

MEMBRANEBLUE™
0.15%
(trypan blue ophthalmic solution) +

Staining solution for intraocular use
Solution colorante pour l'utilisation intraoculaire
Solución tintada para uso intraocular

US Patents
6,696,430 and 6,372,449

MEMBRANEBLUE™
0.15%
(trypan blue ophthalmic solution)

Manufactured by
DORC
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DORC

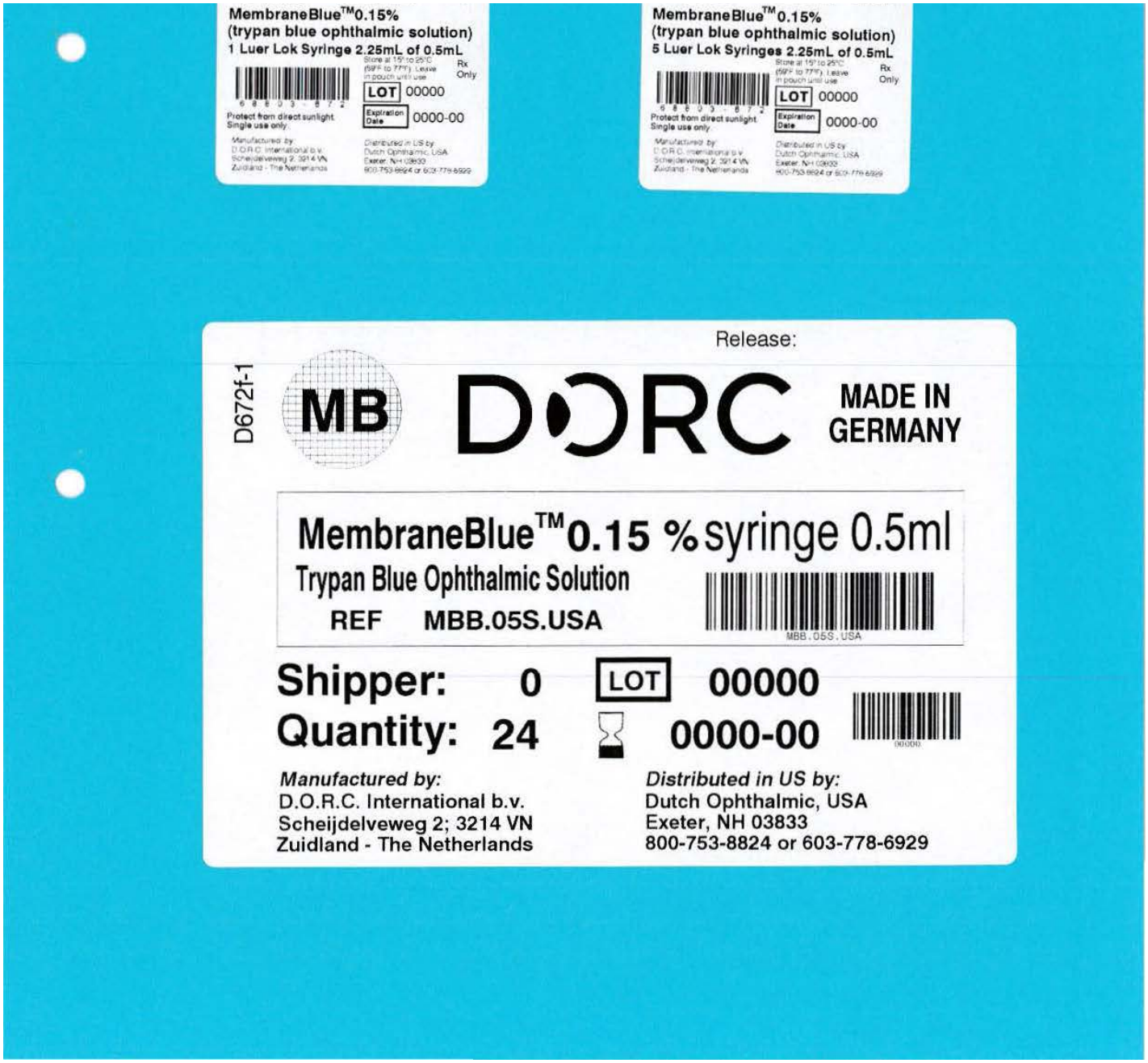
MEMBRANEBLUE™
0.15%
(trypan blue ophthalmic solution)

DORC D672a-1
68803-672
MembraneBlue™ 0.15%
(trypan blue ophthalmic solution)
Single use only 0.5 mL Syringe
STERILE Rx Only LOT
See package insert for dosing information. Protect from direct sunlight.
Expiration Date
Manufactured by: D.O.R.C. International b.v. Scheijdelveweg 2 3214 VN Zuidland, The Netherlands
Distributed in US by: Dutch Ophthalmic USA, Exeter NH 03833 800-753-8824 or 603-778-6929

MembraneBlue™ 0.15%
(trypan blue ophthalmic solution)
LOT 00000 Expiration Date 0000-00
Dutch Ophthalmic USA, Exeter NH 03833
800-753-8824 or 603-778-6929
D672c-1

DORC STERILE D672g-1

DORC STERILE D672b-1



MEMBRANEBLUE

trypan blue injection, solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:68803-672
Route of Administration	OPHTHALMIC, INTRAOCULAR		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
TRYPAN BLUE (UNII: I2ZWO3LS3M) (TRYPAN BLUE FREE ACID - UNII:768N7QO4KH)	TRYPAN BLUE	0.75 mg in 0.5 mL

Inactive Ingredients

Ingredient Name	Strength
SODIUM PHOSPHATE, MONOBASIC, DIHYDRATE (UNII: 5QWK665956)	0.15 mg in 0.5 mL
WATER (UNII: 059QF0KO0R)	0.5 mL in 0.5 mL
SODIUM PHOSPHATE, DIBASIC, DIHYDRATE (UNII: 94255I6E2T)	0.95 mg in 0.5 mL
SODIUM CHLORIDE (UNII: 451W47IQ8X)	4.1 mg in 0.5 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:68803-672-05	5 in 1 CARTON	02/20/2009	
1		1 in 1 POUCH		
1		0.5 mL in 1 SYRINGE, GLASS; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA022278	02/20/2009	

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

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

Establishment

Name	Address	ID/FEI	Business Operations
Pharmpur GmbH		340805167	manufacture(68803-672)

Revised: 11/2021 Dutch Ophthalmic Research Center (International) B.V.