VISIONBLUE® - trypan blue injection, solution
D.O.R.C. Dutch Ophthalmic Research Center (International) B.V.

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use VISIONBLUE® 0.06% safely and effectively. See full prescribing information for VISIONBLUE® 0.06%. VisionBlue® (trypan blue ophthalmic solution) 0.06% Initial U.S. Approval: 2004

INDICATIONS AND USAGE

VisionBlue® 0.06% is an acid di-azo group dye indicated for use as an aid in ophthalmic surgery by staining the anterior capsule of the lens.

DOSAGE AND ADMINISTRATION

- Inject an air bubble into the anterior chamber;
- Carefully apply VisionBlue® 0.06% onto the lens capsule;
- Remove all excess dye from the anterior chamber.

DOSAGE FORMS AND STRENGTHS

VisionBlue® (trypan blue ophthalmic solution) 0.06% 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 VisionBlue® 0.06% should be removed from the eye immediately after staining.

ADVERSE REACTIONS

Inadvertent staining of the posterior lens capsule and vitreous face.

USE IN SPECIFIC POPULATIONS

Trypan blue should not be given to pregnant women.

Revised: 12/2012

FULL PRESCRIBING INFORMATION: CONTENTS*

VisionBlue 0.06% - Indications & Usage Section
VisionBlue 0.06% - Dosage & Administration Section
VisionBlue 0.06% - Dosage forms & Strengths section
VisionBlue 0.06% - Contraindications section
VisionBlue 0.06% - Warnings and Precautions section
VisionBlue 0.06% - Adverse Reactions section
VisionBlue 0.06% - Use in specific populations section
  VisionBlue 0.06% - Pregnancy section
  VisionBlue 0.06% - Nursing Mothers section
  VisionBlue 0.06% - Pediatric use section
  VisionBlue 0.06% - Geriatric use section
VisionBlue 0.06% - Description section
VisionBlue 0.06% - Clinical Pharmacology section
  VisionBlue 0.06% - Mechanism of action section
VisionBlue 0.06% - Nonclinical toxicology section
  VisionBlue 0.06% - Carcinogenesis & Mutagenesis & Impairment of fertility section
VisionBlue 0.06% - How supplied section
* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

VisionBlue 0.06% - Indications & Usage Section
VisionBlue® 0.06% is indicated for use as an aid in ophthalmic surgery by staining the anterior capsule of the lens.

VisionBlue 0.06% - Dosage & Administration Section
Cataract surgery.
VisionBlue® 0.06% is packaged in a 2.25 mL syringe to which a blunt cannula has to be attached.
After opening the eye, an air bubble is injected into the anterior chamber of the eye in order to minimize dilution of VisionBlue® 0.06% by the aqeous. VisionBlue® 0.06% is carefully applied onto the anterior lens capsule using a blunt cannula. Sufficient staining is achieved as soon as the dye has contacted the capsule. The anterior chamber is then irrigated with balanced salt solution to remove all excess dye. An anterior capsulotomy can then be performed.

VisionBlue 0.06% - Dosage forms & Strengths section
VisionBlue® 0.06% is supplied in 2.25 mL syringes filled to a volume of 0.5 mL.

VisionBlue 0.06% - Contraindications section
VisionBlue® 0.06% 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.

VisionBlue 0.06% - Warnings and Precautions section
Excessive staining:
It is recommended that after injection all excess VisionBlue® 0.06% is immediately removed from the eye by thorough irrigation of the anterior chamber.

VisionBlue 0.06% - Adverse Reactions section
Adverse reactions reported following use of VisionBlue® 0.06% 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.

VisionBlue 0.06% - Use in specific populations section

VisionBlue 0.06% - 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 10,000- and 5,000-fold the maximum recommended human dose of 0.3 mg per injection based in 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 20th to 25th days of pregnancy, but no apparent increase in birth defects (approximately 10,000-fold the maximum recommended human daily dose of 0.3 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.

**VisionBlue 0.06% - 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.

**VisionBlue 0.06% - 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.

**VisionBlue 0.06% - Geriatric use section**

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

**VisionBlue 0.06% - Description section**

VisionBlue® (trypan blue ophthalmic solution) 0.06% is a sterile solution of trypan blue (an acid di-azo group dye). VisionBlue® 0.06% is a selective tissue staining agent for use as a medical aid in ophthalmic surgery.

Each mL of VisionBlue® 0.06% contains: 0.6 mg trypan blue; 1.9 mg sodium mono-hydrogen orthophosphate (Na$_2$HPO$_4$·2H$_2$O); 0.3 mg sodium di-hydrogen orthophosphate (NaH$_2$PO$_4$·2H$_2$O); 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$_6$Na$_4$O$_{14}$S$_4$, and has the following chemical structure:

![Chemical structure of trypan blue](image)

**VisionBlue 0.06% - Clinical Pharmacology section**

**VisionBlue 0.06% - Mechanism of action section**

VisionBlue® 0.06% selectively stains connective tissue structures in the human eye such as the anterior lens capsule of the human crystalline lens.

VisionBlue® 0.06% is intended to be applied directly on the anterior lens capsule, staining any portion of the capsule which comes in contact with the dye. Excess dye is washed out of the anterior chamber. The dye does not penetrate the capsule, permitting visualization of the anterior capsule in contrast to the
non-stained lens cortex and inner lens material.

**VisionBlue 0.06% - Nonclinical toxicology section**

**VisionBlue 0.06% - Carcinogenesis & Mutagenesis & Impairment of fertility section**

Trypan blue is carcinogenic in rats. Wistar/Lewis rats developed lymphomas after receiving subcutaneous injections of 1% trypan blue dosed at 50 mg/kg every other week for 52 weeks (total does approximately 250,000-fold the maximum recommended human dose of 0.3 mg per injection in a 60 kg person, assuming total absorption).

Trypan blue was mutagenic in the Ames test and caused DNA strand breaks in vitro.

**VisionBlue 0.06% - How supplied section**

VisionBlue® 0.06% is supplied as follows:

0.5 mL of VisionBlue® 0.06% 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. Ten pouched products are packed in on distribution box.

**VisionBlue 0.06% - Storage and Handling section**


**VisionBlue 0.06% - Patient counseling information**

Patients should be advised that if a non-hydrated, hydrophilic acrylic intraocular lens (IOL) is inserted into their eye, it may absorb the dye and become stained.

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 of 603-778-6929
US Patents 6,367,480 and 6,720,314
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**VisionBlue 0.06% - Package label.Principal display panel**
VisionBlue® 0.06% Trypan Blue Ophthalmic Solution
Single use only
0.5 mL Syringe

DORC
Sterile
08802-012

D412-4

VisionBlue® 0.06% Trypan Blue Ophthalmic Solution
10 Luer Lok 2.25mL Syringes of 0.5mL

Store at 15° to 25°C (59°F to 77°F). Leave in pouch until use.

Rx: Only

LOT 00000
Expiration Date 00000-00

Distributed in U.S.A. by:
DORC International, Inc.
3520 Fryarn Road
Erie, PA 16510
(800) 773-0824 or (814) 772-6905

Manufactured by:
DORC International bv
Schenijnpromenade 2, 3521TV
Eendbergen - The Netherlands

08802-012

VisionBlue® 0.06% Trypan Blue Ophthalmic Solution
1 Luer Lok 2.25mL Syringe of 0.5mL

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Rx: Only

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Manufactured by:
DORC International bv
Schenijnpromenade 2, 3521TV
Eendbergen - The Netherlands

08802-012
VisionBlue® 0.06% syringe 0.5mL
Trypan Blue Ophthalmic Solution
VBL-10S.USA

Shipper: 000
Quantity: 12
LOT 00000
0000-00

Manufactured by:
D.O.R.C International b.v.
Scheijdelweg 2; 3214 VN
Zuidland - The Netherlands

Distributed in US by:
Dutch Ophthalmic, USA
Exeter, NH 03833
(800) 753-8824 or (603) 778-6929
# VISIONBLUE

**trypan blue injection, solution**

## Product Information

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<th>Item Code (Source)</th>
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<td>HUMAN PRESCRIPTION DRUG</td>
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<tr>
<td>INTRAOCULAR, OPHTHALMIC</td>
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## Active Ingredient/Active Moiety

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<tr>
<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
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<tbody>
<tr>
<td>TRYPAN BLUE (UNII: I2ZWO3LS3M) (TRYPAN BLUE FREE ACID - UNII:768N7Q04KH)</td>
<td>TRYPAN BLUE</td>
<td>0.3 mg in 0.5 mL</td>
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## Inactive Ingredients

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<tr>
<th>Ingredient Name</th>
<th>Strength</th>
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<tbody>
<tr>
<td>SODIUM PHOSPHATE, MONOBASIC, DIHYDRATE (UNII: 5QWK665956)</td>
<td>0.15 mg in 0.5 mL</td>
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<td>SODIUM PHOSPHATE, DIBASIC, DIHYDRATE (UNII: 94255I6E2T)</td>
<td>0.85 mg in 0.5 mL</td>
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<tr>
<td>SODIUM CHLORIDE (UNII: 451W47Q8X)</td>
<td>4.1 mg in 0.5 mL</td>
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<tr>
<td>WATER (UNII: 059QF0KO0R)</td>
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## Packaging

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<td>10 in 1 CARTON</td>
<td>12/16/2014</td>
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<td>1</td>
<td></td>
<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
- D.O.R.C. Dutch Ophthalmic Research Center (International) B.V. (407522184)

### Registrant
- D.O.R.C. Dutch Ophthalmic Research Center (International) B.V. (407522184)

### Establishment

<table>
<thead>
<tr>
<th>Name</th>
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<tr>
<td>Pharmpur GmbH</td>
<td></td>
<td>340805167</td>
<td>manufacture(68803-612)</td>
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