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

HIGHLIGHTS OF PRESCRIBING INFORMATION
VisionBlue® 0.06% Trypan blue Ophthalmic Solution. 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

HIGHLIGHTS OF PRESCRIBING INFORMATION (1)
These highlights do not include all the information needed to use VISIONBLUE® safely and effectively. See full prescribing information for VISIONBLUE®. VisionBlue® (trypan blue ophthalmic solution) 0.06% Initial U.S. Approval: 2004 (1)
(1)
VisionBlue® 0.06% is a diagnostic dye indicated for use as an aid in ophthalmic surgery by staining the anterior capsule of the lens. (1)

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 single-patient-use syringe. (3)

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

Excessive staining: Excess VisionBlue® 0.06% should be removed from the eye immediately after staining. (5)

ADVERSE REACTIONS

Inadvertent staining of the posterior lens capsule and vitreous face. (6)
(6)
To report SUSPECTED ADVERSE REACTIONS contact, Dutch Ophtalmic, USA at 1-800-75-DUTCH or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch (6)

Revised: 12/2012

FULL PRESCRIBING INFORMATION: CONTENTS*

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 single-patient-use syringe filled to a volume of 0.5 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 aqueous. 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® (trypan blue ophtalmic solution) 0.06% is a clear, dark blue ophtalmic solution supplied in 2.25 mL single-patient-use syringe 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

Risk Summary

There are no available data on the use of VisionBlue® 0.06% in pregnant women to inform a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Systemic absorption of VisionBlue® 0.06% in humans is expected to be negligible following injection and subsequent removal of the drug at the completion of surgical procedures. Adequate animal reproduction studies were not conducted with VisionBlue® 0.06%, however, trypan blue has been shown to be teratogenic in various animal models at doses 800-fold and greater than the maximum recommended human dose, based on body surface area (BSA).

Due to the negligible human systemic exposure when used as recommended, it is not expected that maternal use of VisionBlue® 0.06% will result in fetal exposure to the drug and risk of teratogenic effects.

Animal Data

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. Normalized to BSA, these doses are approximately 1,600- and 800-fold the maximum recommended human dose of 0.3 mg per injection (based on a 60 kg person), assuming complete systemic absorption of trypan blue. 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 3,200-fold the maximum recommended human dose based on BSA, assuming total absorption).

VisionBlue 0.06% - Nursing Mothers section

Risk Summary

The presence of trypan blue in human milk following intraocular administration of trypan blue has not been evaluated. There are no data available regarding the effects of trypan blue on milk production. Breastfeeding is not expected to result in exposure of the child to trypan blue due to the negligible systemic exposure of trypan blue in humans following injection and subsequent removal of the drug at the completion of surgical procedures.

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

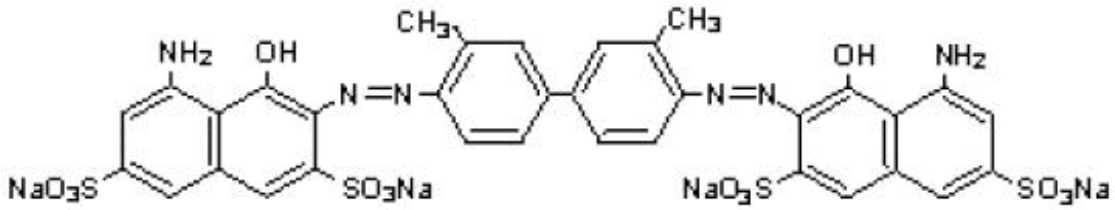
No overall differences in safety and effectiveness have been observed between elderly and younger patients.

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) for intraocular ophtalmic use. 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 ($Na_2HPO_4 \cdot 2H_2O$); 0.3 mg sodium di-hydrogen orthophosphate ($NaH_2PO_4 \cdot 2H_2O$); 8.2 mg sodium chloride (NaCl); and water for injection. Sodium hydroxide may be used to adjust pH. 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:



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

Carcinogenesis, mutagenesis, impairment of fertility

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 42,000-fold the maximum recommended human dose of 0.3 mg per injection in a 60 kg person based on BSA, 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 a clear, dark blue ophtalmic solution supplied as follows:

0.5 mL of VisionBlue® 0.06% in a sterile single-patient-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 one distribution box.

NDC 68803-612-05 (One 0,5 mL syringe)

NDC 68803-612-10 (Carton of ten 0.5 mL syringes)

VisionBlue 0.06% - Storage and Handling section

Store between 15-25°C (59-77°F). Protect form direct sunlight.

VisionBlue 0.06% - Patient counseling information

Advise patients 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

VisionBlue 0.06% - Package label.Principal display panel

D642e-4

DORC

VISIONBLUE®
SYRINGE

0.06% Trypan Blue
Ophthalmic Solution

DORC

See package insert for dosing information

Leave syringe in pouch until use. Protect from light, frost and moisture. Store at 15˚C to 25˚C (59˚F to 77˚F). Sterile.

Active ingredients: Trypan blue 0.06%.

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

Labeler code no.: 68803-612 Rx ONLY

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

DORC

VISIONBLUE®
SYRINGE

0.06% Trypan Blue
Ophthalmic Solution

Manufactured by
DORC
Dutch Ophthalmic Research Center International BV
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The Netherlands

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

DORC

VISIONBLUE®
SYRINGE

0.06% Trypan Blue
Ophthalmic Solution

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

US Patents
6,367,480 and 6,720,314

DORC

VISIONBLUE®
SYRINGE

0.06% Trypan Blue
Ophthalmic Solution

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Exeter, NH 03833, USA
Phone: 800-75-DUTCH or 603-778-6929


D642b-4
68803-612
VisionBlue® 0.06% 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


VisionBlue® 0.06% Trypan Blue Ophthalmic Solution
LOT
00000
Expiration Date
0000-00
Dutch Ophthalmic, USA, Exeter, NH 03833
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D642c-4


D•ORC
STERILE
D642b-4
VisionBlue® 0.06% Trypan Blue Ophthalmic Solution
10 Luer Lok 2.25mL Syringes of 0.5mL
68803-612
Protect from direct sunlight.
Single use only.
Store at 15° to 25°C (59°F to 77°F). Leave in pouch until use.
Rx Only
LOT
00000
Expiration Date
0000-00
Manufactured by:
D.O.R.C. International b.v.
Scheijdelveweg 2; 3214 VN
Zuidland – The Netherlands
Distributed in US by:
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(800) 753-8824 or (603) 778-6929


D•ORC
STERILE
D642g-4
VisionBlue® 0.06% Trypan Blue Ophthalmic Solution
1 Luer Lok 2.25mL Syringe of 0.5mL
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Protect from direct sunlight.
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0000-00
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(800) 753-8824 or (603) 778-6929

Release:

D642f-4

MADE IN GERMANY

D)RC

VisionBlue® 0.06% syringe 0.5mL

Trypan Blue Ophthalmic Solution

VBL-10S.USA

VBL-10S.USA

Shipper: 000

LOT **00000**

00000

Quantity: 12

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

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VISIONBLUE

trypan blue injection, solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:68803-612
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	0.3 mg in 0.5 mL

Inactive Ingredients	
Ingredient Name	**Strength**
SODIUM PHOSPHATE, MONOBASIC, DIHYDRATE (UNII: 5QWK665956)	0.15 mg in 0.5 mL
SODIUM PHOSPHATE, DIBASIC, DIHYDRATE (UNII: 94255I6E2T)	0.85 mg in 0.5 mL
SODIUM CHLORIDE (UNII: 451W47IQ8X)	4.1 mg in 0.5 mL
WATER (UNII: 059QF0KO0R)	0.5 mL in 0.5 mL

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:68803-612-10	10 in 1 CARTON	12/16/2004	
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	NDA021670	12/16/2004	

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

Name	Address	ID/FEI	Business Operations
Pharmpur GmbH		340805167	manufacture(68803-612)