

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-670

APPROVED LABELING

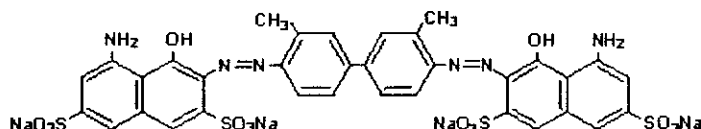
VisionBlue[®] (trypan blue ophthalmic solution)

Description

VisionBlue[®] (trypan blue ophthalmic solution) 0.06% is a sterile solution of trypan blue (an acid di-azo group dye). VisionBlue[®] 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 (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 mOsm/kg.

The drug substance trypan blue has the chemical name 3,3'-[(3,3'-dimethyl-4,4'-biphenylene) bis (azo)] bis(5-amino-4-hydroxy-2,7-naphthalenedisulfonic acid) tetra sodium salt, a molecular weight of 960.8, a molecular formula of C₃₄H₂₄N₆Na₄O₁₄S₄, and has the following chemical structure:



Clinical Pharmacology

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

VisionBlue[®] 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.

Indications and Usage

VisionBlue[®] is indicated for use as an aid in ophthalmic surgery by staining the anterior capsule of the lens.

Contraindications

VisionBlue[®] is contraindicated when a non-hydrated (dry state), hydrophilic acrylic intraocular lens (IOL) is planned to be inserted into the eye because the dye may be absorbed by the IOL and stain the IOL.

Precautions

General: It is recommended that after injection all excess VisionBlue[®] be immediately removed from the eye by thorough irrigation of the anterior chamber.

Carcinogenesis, mutagenesis, impairment of fertility

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 dose approximately 1,250,000-fold the maximum recommended human dose of 0.06 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.

Pregnancy

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 50,000- and 25,000-fold the maximum recommended human dose of 0.06 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 50,000-fold maximum recommended human dose of 0.06 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.

Nursing mothers

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.

Pediatric use

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.

Geriatric use

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

Adverse Reactions

Adverse reactions reported following use of VisionBlue® 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.

Dosage and Administration

Cataract surgery

VisionBlue® 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® by the aqueous. VisionBlue® is carefully applied onto the anterior lens capsule using a blunt cannula. Sufficient staining is achieved as soon as the dye has contacted the

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capsule. The anterior chamber is then irrigated with balanced salt solution to remove all excess dye. An anterior capsulotomy can then be performed.

How Supplied

VisionBlue® 0.06% is supplied as follows:

0.5 mL of VisionBlue® 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.

Storage


VisionBlue® 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
One Little River Road
P.O. Box 968
Kingston, NH-03848, U.S.A.
Phone: 800-75-DUTCH or 603-642-8468.

Box & Peel Pouch Label

DORC		STERILE	D642b-1
VisionBlue® 0.06% Trypan Blue Ophthalmic Solution			
10 Luer Lok 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 12345		
		Expiration Date	YYYY-MM
Manufactured by: D.O.R.C. International b.v. Scheijdelweg 2; 3214 VN Zuidland - The Netherlands		Distributed in US by: Dutch Ophthalmic, USA Kingston, NH 03848 (800) 753-8824 or (603) 642-8468	

DORC		STERILE	D642f-1
VisionBlue® 0.06% Trypan Blue Ophthalmic Solution			
1 Luer Lok Syringe 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 12345		
		Expiration Date	YYYY-MM
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Syringe Label

DORC	D642a-1
68803-612	
VisionBlue® 0.06% Trypan Blue Ophthalmic Solution	
Single use only 0.5 mL Syringe	
STERILE	Rx Only
LOT	12345
See package insert for dosing information. Protect from direct sunlight.	Expiration Date YYYY-MM
Manufactured by: D.O.R.C. International b.v. Scheijdelweg 2; 3214 VN Zuidland, The Netherlands Distributed in US by: Dutch Ophthalmic, USA, Kingston NH 03848 (800-753-8824 or 603-642-8468)	

Patient Record Label

VisionBlue® 0.06% Trypan Blue Ophthalmic Solution	
LOT 12345	Expiration Date YYYY-MM
Dutch Ophthalmic USA, Kingston NH 03848 (800-753-8824 or 603-642-8468)	

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/s/

Jonca Bull

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