

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® is an acid di-azo group 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. (2)

-----DOSAGE FORMS AND STRENGTHS-----

- VisionBlue® (trypan blue ophthalmic solution) 0.06% 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 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)

To report SUSPECTED ADVERSE REACTIONS contact FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

-----USE IN SPECIFIC POPULATIONS-----

- Trypan blue should not be given to pregnant women. (8.1)

See 17 for PATIENT COUNSELING INFORMATION

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

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

2 DOSAGE AND ADMINISTRATION

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 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.

3 DOSAGE FORMS AND STRENGTHS

VisionBlue® (trypan blue ophthalmic solution) 0.06% is supplied in 2.25 mL syringes filled to a volume of 0.5 mL.

4 CONTRAINDICATIONS

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.

5 WARNINGS AND PRECAUTIONS

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.

6 ADVERSE REACTIONS

Adverse reactions reported following use of VisionBlue® 0.06% include discoloration of high water content hydrogen intraocular lenses [*see Contraindications (4)*] 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.

8 USE IN SPECIFIC POPULATIONS

8.1 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 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 maximum recommended human 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.

8.3 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.

8.4 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.

8.5 Geriatric use

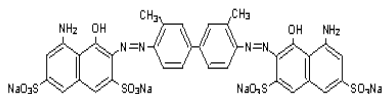
No overall differences in safety and effectiveness have been observed between elderly and younger patients.

11 DESCRIPTION

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 ($\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$); 0.3 mg sodium di-hydrogen orthophosphate ($\text{NaH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O}$); 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'-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 $\text{C}_{34}\text{H}_{24}\text{N}_6\text{Na}_4\text{O}_{14}\text{S}_4$, and has the following chemical structure:



12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

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.

13 NONCLINICAL TOXICOLOGY

13.1 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 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.

16 HOW SUPPLIED/STORAGE AND HANDLING

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 one distribution box.

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

17 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.

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