

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

209569Orig1s000

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use TissueBlue 0.025% safely and effectively. See full prescribing information for TissueBlue 0.025%.

**TissueBlue (Brilliant Blue G Ophthalmic Solution) 0.025%
For Intraocular Ophthalmic Administration
Initial U.S. Approval: 2019**

-----INDICATIONS AND USAGE-----

TissueBlue (Brilliant Blue G Ophthalmic Solution) 0.025% is a disclosing agent indicated to selectively stain the internal limiting membrane (ILM). (1)

-----DOSAGE AND ADMINISTRATION-----

Inject TissueBlue 0.025% directly in a Balanced Salt Solution (BSS)-filled vitreous cavity. (2)
Excess TissueBlue should be removed from the vitreous cavity. (2)

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

TissueBlue (Brilliant Blue G Ophthalmic Solution) 0.025% is supplied in 2.25 mL syringes filled to a volume of 0.5 mL. (3)

-----CONTRAINDICATIONS-----

None (4)

-----WARNINGS AND PRECAUTIONS-----

Excessive staining: Excess TissueBlue 0.025% should be removed from the eye immediately after staining. (5.1)
Use of the syringe: Make sure the plunger moves smoothly before injecting the solution. (5.2)

-----ADVERSE REACTIONS-----

Adverse reactions that have been reported in procedures that included the use of TissueBlue 0.025% have often been associated with the surgical procedure. The complications include retinal (retinal break, tear, hemorrhage, and detachment and cataracts. (6)

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

Revised: 12/2019

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

TissueBlue (Brilliant Blue G Ophthalmic Solution) 0.025% is indicated to selectively stain the internal limiting membrane (ILM).

2 DOSAGE AND ADMINISTRATION

TissueBlue 0.025% is carefully injected into the Balanced Salt Solution (BSS)-filled vitreous cavity using a blunt cannula attached to the pre-filled syringe, without allowing the cannula to contact the retina or allowing TissueBlue to get under the retina. Sufficient staining is expected within a few seconds. Following staining, all excess dye should be removed from the vitreous cavity.

3 DOSAGE FORMS AND STRENGTHS

TissueBlue (Brilliant Blue G Ophthalmic Solution) 0.025% is a clear, bright blue, single-dose ophthalmic solution supplied in 2.25 mL syringes pre-filled to a volume of 0.5 mL.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Excessive Staining

Excess TissueBlue 0.025% should be removed from the eye immediately after staining.

5.2 Use of the Syringe

Make sure the plunger moves smoothly before injecting the solution. Do not use the product if the plunger does not move smoothly to prime the cannula.

6 ADVERSE REACTIONS

Adverse reactions that have been reported in procedures that included the use of Brilliant Blue G Ophthalmic Solution have often been associated with the surgical procedure. These complications include retinal (retinal break, tear, hemorrhage, and detachment) and cataracts.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on the use of TissueBlue 0.025% in pregnant women to inform a drug associated risk. Systemic absorption of TissueBlue 0.025% in humans is expected to be negligible following intravitreal injection and subsequent removal of the drug at the completion of surgical procedures. Due to the negligible systemic exposure, it is not expected that maternal use of TissueBlue 0.025% will result in fetal exposure to the drug.

Adequate animal reproduction studies were not conducted with TissueBlue 0.025%.

8.2 Lactation

Risk Summary

No data are available regarding the presence of Brilliant Blue G in human milk after intraocular administration of TissueBlue 0.025%, or the effects on the breastfed infant or the effects on milk production. However, breastfeeding is not expected to result

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Silver Spring, MD 20993

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in exposure of the child to Brilliant Blue G due to the expected negligible systemic exposure of BBG in humans following intravitreal injection and subsequent removal of the drug at the completion of surgical procedures.

8.4 Pediatric Use

The safety and effectiveness of TissueBlue 0.025% in pediatric patients has not been established.

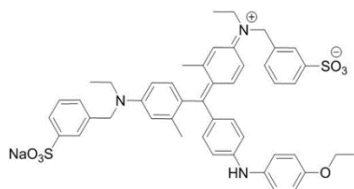
8.5 Geriatric Use

No overall differences in safety or effectiveness were observed between elderly and younger adult patients.

11 DESCRIPTION

TissueBlue (Brilliant Blue G Ophthalmic Solution) 0.025% is a sterile solution of BBG (a dye). Each mL of TissueBlue 0.025% contains BBG 0.25 mg, Polyethylene Glycol 40mg and Buffered Sodium Chloride solution (8.20 mg of sodium chloride, 3.10 mg sodium phosphate dibasic dodecahydrate, 0.30 mg sodium phosphate monobasic dihydrate, water for injection). The pH range of TissueBlue 0.025% Solution is between 7.3 and 7.6.

The drug substance BBG has the chemical name Brilliant Blue G, a molecular weight of 854.02 and has the following chemical structure:



Molecular formula: $C_{47}H_{48}N_3NaO_7S_2$

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Brilliant Blue G has been shown to selectively stain the ILM, but not the epiretinal membrane nor the retina, making it easier to visualize the membrane for removal, although the exact mechanism of this selectivity has not been elucidated.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies to evaluate the potential for carcinogenicity or impairment of fertility of TissueBlue 0.025% have not been conducted. Brilliant Blue G was not mutagenic in the Ames assay, the *in vitro* mouse lymphoma assay, or the *in vivo* rat micronucleus assay.

16 HOW SUPPLIED/STORAGE AND HANDLING

TissueBlue (Brilliant Blue G Ophthalmic Solution), 0.025% is supplied as 0.5 mL of Brilliant Blue G Ophthalmic Solution, 0.025% in a sterile, single-dose Luer Lok, 2.25 mL glass syringe, with a grey rubber plunger stopper and tip cap with polypropylene plunger rod in a pre-formed polypropylene blister pouch sealed with a Tyvek® lid.

NDC 68803-722-05 (One 0.5 mL syringe)

NDC 68803-722-25 (Carton of five 0.5 mL syringes)

TissueBlue 0.025% should be stored at 15°C to 25°C (59°F to 77°F). Protect from light, frost and moisture.

Rx Only

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NDA 209569

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

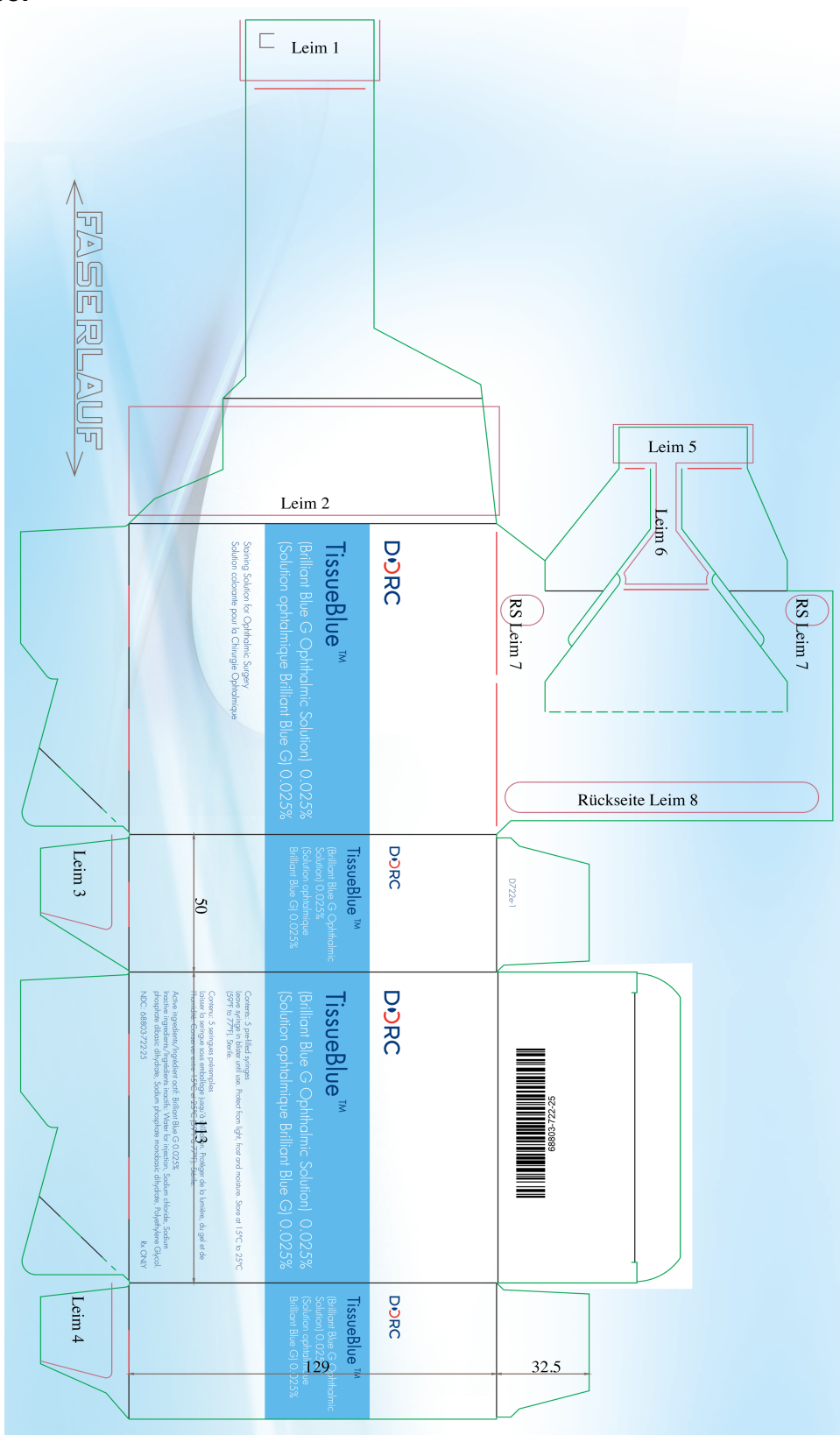
Revision Date: 12/2019

Made in Germany

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Silver Spring, MD 20993
www.fda.gov

5 Unit Carton Label



Carton End Label

DORC



D722b-1

TissueBlue™

(Brilliant Blue G Ophthalmic Solution) 0.025%
(Solution ophtalmique Brilliant Blue G) 0.025%

5 Luer Lock 2.25mL Syringes of 0.5mL

LOT 12345

EXP. YYYY-MM

Distributed in US by:

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Exeter, NH 03833

Distributed in Canada by:

INNOVA MEDICAL OPHTHALMICS
48 Camforth Rd, Toronto, Ontario,
M4A 2K7, Canada

Store at 15°C to 25°C (59°F to 77°F). Protect from light, frost and moisture. Leave in blister until use. Sterile. Single use only.

Conserver entre 15°C et 25°C (59°F à 77°F). Protéger de la lumière, due gel et de l'humidité. Stérile. Laisser sous emballage jusqu' à utilization. Usage unique.

Patient Record Label

TissueBlue™
(Brilliant Blue G Ophthalmic Solution) 0.025%
(Solution ophtalmique Brilliant Blue G) 0.025%

LOT 12345 **EXP.** YYYY-MM

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48 Camforth Rd, Toronto, Ontario, M4A 2K7, Canada

D722c-1

Tyvek Syringe Blister Label

TissueBlue™ NDC: 68803-722-05
(Brilliant Blue G Ophthalmic Solution) 0.025% **DORC**

1 Luer Lock 2.25mL Syringe of 0.5mL

LOT 12345
EXP. YYYY - MM

STERILE 

Store at 15°C to 25°C (59°F to 77°F).
Protect from light, frost and moisture.
Leave in blister until use. Single use only.

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48 Camforth Rd, Toronto, Ontario

D722h-1

Syringe Label

DORC

D722a-2

TissueBlue™

NDC: 68803-722-05

(Brilliant Blue G Ophthalmic Solution) 0.025%
(Solution ophtalmique Brilliant Blue G) 0.025%

0.5 mL Syringe

Rx Only

Single use only
Usage Unique

See package insert for
dosing information
Voir la notice pour les
informations de dosage

STERILE 

LOT

12345

Protect from light, frost
and moisture
Protéger de la lumière, du
gel et de l'humidité

EXP.

YYYY - MM

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/s/

PETER P STEIN
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