LYMPHAZURIN- isosulfan blue injection, solution
UNITED STATES SURGICAL CORPORATION

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LYMPHAZURIN safely and effectively. See full prescribing information for LYMPHAZURIN.

LYMPHAZURIN injection, solution for subcutaneous use
Initial U.S. Approval: 1981

RECENT MAJOR CHANGES

Warnings and Precautions, Interference with Oxygen Saturation and Methemoglobin Measurements (5.3). 10/2007

INDICATIONS AND USAGE

Lymphazurin™ 1% (isosulfan blue) upon subcutaneous administration, delineates the lymphatic vessels draining the region of injection. It is an adjunct to lymphography in: primary and secondary lymphedema of the extremities; chyluria, chylous ascites or chylothorax; lymph node involvement by primary or secondary neoplasm; lymph node response to therapeutic modalities (1.1).

DOSAGE AND ADMINISTRATION

Lymphazurin™ 1% is to be administered subcutaneously, one-half (1/2) ml into three (3) interdigital spaces of each extremity per study. A maximum dose of 3 ml (30 mg) isosulfan blue is, therefore, injected (2.1).

DOSAGE FORMS AND STRENGTHS

1% aqueous solution (isosulfan blue) (3)

CONTRAINDICATIONS

Hypersensitivity to triphenylmethane or related compounds (4).

WARNINGS AND PRECAUTIONS

- Life-threatening anaphylactic reactions have occurred after Lymphazurin 1% administration. Monitor patients closely for at least 60 minutes after administration of Lymphazurin 1% (5.1).
- The admixture of Lymphazurin 1% with local anesthetics results in an immediate precipitation of 4-9% drug complex. Use a separate syringe for anesthetics (5.2).
- Lymphazurin 1% interferes with measurements in peripheral blood pulse oximetry. Arterial blood gas analysis may be needed (5.3).

ADVERSE REACTIONS

Hypersensitivity reactions: Hypersensitivity reactions occurring approximately 2% of patients and include life-threatening anaphylactic reactions with respiratory distress, shock, angioedema, urticaria, pruritus. A death has been reported following IV administration of a similar compound (6).

To report SUSPECTED ADVERSE REACTIONS, contact U.S. Surgical at 1-800-522-0263 option 5 and website or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

DRUG INTERACTIONS

No drug interactions have been identified for Lymphazurin 1% (7).

USE IN SPECIFIC POPULATIONS

- Caution should be exercised when Lymphazurin 1% is administered to nursing mothers (8.3).
- Safety and effectiveness of Lymphazurin 1% in children has not been established (8.4).

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 1/2012

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Lymphatic Vessel Delineation

Lymphazuirn™ 1% (isosulfan blue) upon subcutaneous administration, delineates lymphatic vessels draining the region of injection. It is an adjunct to lymphography in: primary and secondary lymphedema of the extremities; chyluria, chylous ascites or chylothorax; lymph node involvement by primary or secondary neoplasm; and lymph node response to therapeutic modalities.

2 DOSAGE AND ADMINISTRATION

2.1 Subcutaneous administration

Lymphazurin™ 1% is to be administered subcutaneously, one-half (1/2) ml into three (3) interdigital spaces of each extremity per study. A maximum dose of 3 ml (30 mg) isosulfan blue is, therefore, injected.

3 DOSAGE FORMS AND STRENGTHS

1% aqueous solution (isosulfan blue)

4 CONTRAINDICATIONS

Lymphazurin™ 1% (isosulfan blue) is contraindicated in those individuals with known hypersensitivity to triphenylmethane or related compounds.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Life-threatening anaphylactic reactions (respiratory distress, shock, angioedema) have occurred after Lymphazurin 1% administration. Reactions are more likely to occur in patients with a history of bronchial asthma, allergies, drug reactions or previous reactions to triphenylmethane dyes. Monitor patients closely for at least 60 minutes after administration of Lymphazurin 1%. Trained personnel should be available to administer emergency care including resuscitation.

5.2 Precipitation of Lymphazurin 1% by Lidocaine

The admixture of Lymphazurin 1% (with local anesthetics (i.e. lidocaine)) in the same syringe results in an immediate precipitation of 4 – 9% drug complex. Use a separate syringe to administer a local anesthetic.

5.3 Interference with Oxygen Saturation and Methemoglobin Measurements

Lymphazurin 1% interferes with measurements of oxygen saturation in peripheral blood by pulse oximetry and can cause falsely low readings. The interference effect is maximal at 30 minutes and minimal generally by four hours after administration. Arterial blood gas analysis may be needed to verify decreased arterial partial pressure of oxygen.

Lymphazurin 1% may also cause falsely elevated readings of methemoglobin by arterial blood gas analyzer. Therefore, co-oximetry may be needed to verify methemoglobin level.

6 ADVERSE REACTIONS

6.1 Postmarketing Experience

Hypersensitivity Reactions: Case series report an overall incidence of hypersensitivity reactions in approximately 2% of patients. Life-threatening anaphylactic reactions have occurred. Manifestations include respiratory distress, shock, angioedema, urticaria, pruritus. A death has been reported following administration of a similar compound employed to estimate the depth of a severe burn. Reactions are more likely to occur in patients with a personal or family history of bronchial asthma, significant allergies, drug reactions or previous reactions to triphenylmethane dyes [see Warnings and Precautions (5)].

Laboratory tests: Lymphazurin 1% interferes with measurements of oxygen saturation by pulse oximetry and of methemoglobin by gas analyzer [see Warnings and Precautions (5)].

Skin: transient or long-term (tattooing) blue coloration.

7 DRUG INTERACTIONS

No Drug Interactions have been identified with Lymphazurin 1%.

8 USE IN SPECIFIC POPULATIONS

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 Lymphazurin™ 1% (isosulfan blue) is administered to a nursing mother.

8.4 Pediatric Use

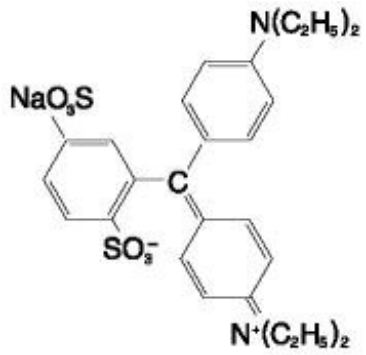
Safety and effectiveness of Lymphazurin™ 1% (isosulfan blue) in children have not been established.

10 OVERDOSAGE

Do not exceed indicated recommended dosage as overdosage levels have not been identified for Lymphazurin 1%.

11 DESCRIPTION

The chemical name of Lymphazurin 1% (isosulfan blue) is N-[4-[[4-(diethylamino)phenyl] (2,5-disulfophenyl) methylene]-2,5-cyclohexadien-1-ylidene]-N-ethylehananamunium hydroxide, inner salt, sodium salt. Its structural formula is:



Lymphazurin 1% is a sterile aqueous solution for subcutaneous administration. Phosphate buffer in sterile, pyrogen free water is added in sufficient quantity to yield a final pH of 6.8-7.4. Each ml of solution contains 10 mg Isosulfan blue, 6.6 mg sodium monohydrogen phosphate and 2.7 mg potassium dihydrogen phosphate. The solution contains no preservative. Lymphazurin 1% is a contrast agent for the delineation of lymphatic vessels.

12 CLINICAL PHARMACOLOGY

12.2 Pharmacodynamics

Following subcutaneous administration, Lymphazurin 1% binds to serum proteins and is picked up by the lymphatic vessels. Thus, the lymphatic vessels are delineated by the blue dye.

12.3 Pharmacokinetics

Up to 10% of the subcutaneously administered dose of Lymphazurin 1% is excreted unchanged in the urine in 24 hours in human.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals have not been performed to evaluate the carcinogenic potential of Lymphazurin 1%. Reproduction studies in animals have not been conducted and, therefore, it is unknown if a problem concerning mutagenesis or impairment of fertility in either males or females exists.

13.2 Teratogenic Effects

Pregnancy Category C. Animal reproduction studies have not been conducted with Lymphazurin 1%. It is not known whether Lymphazurin 1% can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Lymphazurin 1% should be given to a pregnant woman only if clearly needed.

16 HOW SUPPLIED/STORAGE AND HANDLING

Lymphazurin 1% is supplied as a 5 ml single dose vial, 1% aqueous solution in a phosphate buffer prepared by appropriate manufacturing to be sterile and pyrogen-free.

17 PATIENT COUNSELING INFORMATION

Inform patients that urine color may be blue for 24 hours following administration of Lymphazurin 1%.

PRINCIPAL DISPLAY PANEL

D.I.N. 00592358
NDC 63261-250-21 LYM-100
LYMPHAZURIN* 1%
(isosulfan blue) Single Dose Vial 5 ml.

Mfd. for United States Surgical, a division of
Tyco Healthcare Group LP,
Norwalk, CT 06856 USA.

by Ben Venue Labs, Inc., Bedford, OH 44146 USA

Distributed in Canada by: Tyco Healthcare
Montreal, Quebec
Canada, H9R 5H8

LYMPHAZURIN

isosulfan blue injection, solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:63261-250
Route of Administration	SUBCUTANEOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
ISOSULFAN BLUE (UNII: 39N9K8S2A4) (ISOSULFAN BLUE - UNII:39N9K8S2A4)	ISOSULFAN BLUE	10 mg in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
SODIUM PHOSPHATE, DIBASIC, ANHYDROUS (UNII: 22ADO53M6F)	
POTASSIUM PHOSPHATE, MONOBASIC (UNII: 4J9FJ0HL51)	
WATER (UNII: 059QF0KO0R)	

Product Characteristics			
Color	blue	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:63261-250-21	5 mL in 1 VIAL, SINGLE-USE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA018310	01/12/2012	

Labeler - UNITED STATES SURGICAL CORPORATION (044680650)

Establishment

Name	Address	ID/FEI	Business Operations
BEN VENUE LABORATORIES, INC.		004327953	manufacture

Establishment

Name	Address	ID/FEI	Business Operations

SIGMA-ALDRICH CO LTD		397924143	api manufacture