

**ISOSULFAN BLUE- isosulfan blue injection, solution**  
**Somerset Therapeutics, LLC**

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**HIGHLIGHTS OF PRESCRIBING INFORMATION**

**These highlights do not include all the information needed to use ISOSULFAN BLUE INJECTION, 1% safely and effectively. See full prescribing information for ISOSULFAN BLUE INJECTION 1%.**

**ISOSULFAN BLUE Injection, for subcutaneous use**

**Initial U.S. Approval: 1981**

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**RECENT MAJOR CHANGES**-----

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

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

Isosulfan blue injection 1% 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). (1)

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

Isosulfan blue injection 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). (2)

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

1% aqueous solution (isosulfan blue) (3)

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**CONTRAINDICATIONS**-----

Hypersensitivity to triphenylmethane or related compounds. (4)

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

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

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**ADVERSE REACTIONS**-----

Hypersensitivity Reactions: Hypersensitivity reactions occur in 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 Somerset Therapeutics, LLC at 1- 800-417-9175 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch) (6)**

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**DRUG INTERACTIONS**-----

No drug interactions have been identified for isosulfan blue injection 1%. (7)

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

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

**See 17 for PATIENT COUNSELING INFORMATION.**

**Revised: 7/2018**

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

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## **FULL PRESCRIBING INFORMATION**

### **1 INDICATIONS AND USAGE**

#### **1.1 Lymphatic Vessel Delineation**

Isosulfan blue injection 1% 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**

Isosulfan blue injection 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**

Isosulfan blue injection 1% 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 isosulfan blue injection 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 isosulfan blue injection 1%. Trained personnel should be available to administer emergency care including resuscitation.

### **5.2 Precipitation of Isosulfan Blue Injection 1% by Lidocaine**

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

### **5.3 Interference with Oxygen Saturation and Methemoglobin Measurements**

Isosulfan blue injection 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 4 hours after administration. Arterial blood gas analysis may be needed to verify decreased arterial partial pressure of oxygen.

Isosulfan blue injection 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 Post-Marketing 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: Isosulfan blue injection 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 isosulfan blue injection 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 isosulfan blue injection 1% is administered to a nursing mother.

### **8.4 Pediatric Use**

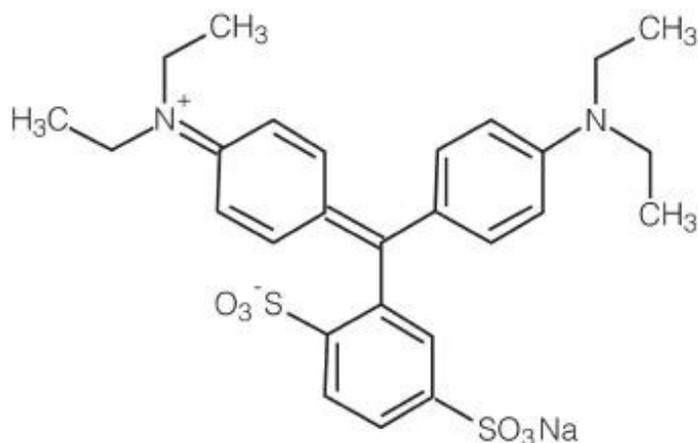
Safety and effectiveness of isosulfan blue injection 1% in children have not been established.

## 10 OVERDOSAGE

Do not exceed indicated recommended dosage as overdose levels have not been identified for isosulfan blue injection 1%.

## 11 DESCRIPTION

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



Isosulfan blue injection 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 to 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. Isosulfan blue injection 1% is a contrast agent for the delineation of lymphatic vessels.

## 12 CLINICAL PHARMACOLOGY

### 12.2 Pharmacodynamics

Following subcutaneous administration, isosulfan blue injection 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 isosulfan blue injection 1% is excreted unchanged in the urine in 24 hours in humans.

## 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 isosulfan blue injection 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.

### 13.3 Teratogenic Effects

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

### 16 HOW SUPPLIED/STORAGE AND HANDLING

Isosulfan blue injection 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.

NDC 70069-221-06

carton containing 6 x 5 mL single-dose vials

**STORAGE: Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature]. Avoid excessive heat.**

### 17 PATIENT COUNSELING INFORMATION

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

#### Manufactured By:

Wintac Limited

Bangalore 562123

India

Code No.: KR/DRUGS/KTK/28/289/97

#### Manufactured for:

Somerset Therapeutics, LLC

Somerset, NJ 08873

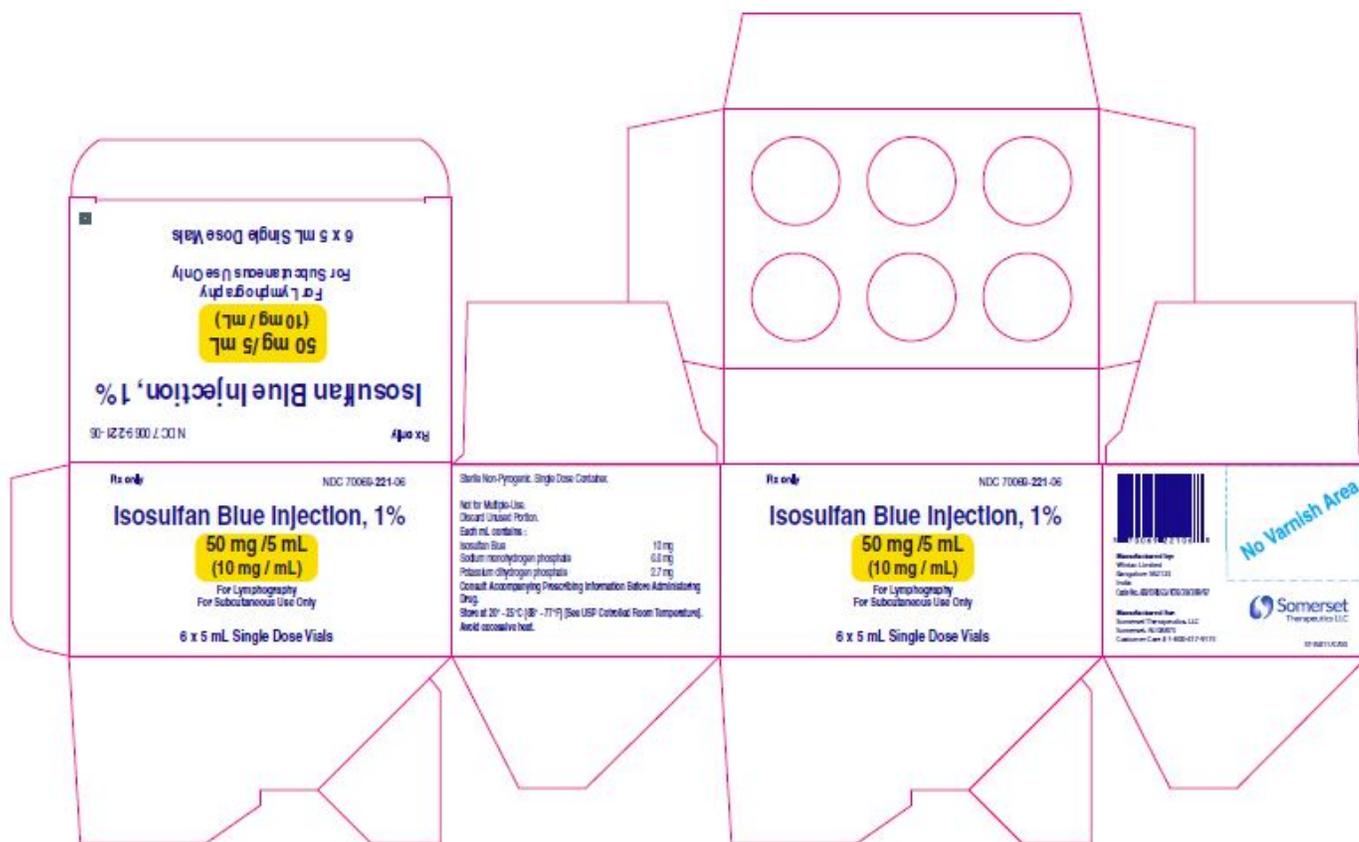
ST-ISB11/P/00

### PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

Container label

<p>Sterile, Non-pyrogenic. Single Dose Container. Contains no preservatives. Discard Unused Portion. Each mL contains : Isosulfan Blue 10 mg Usual Dosage : See Package Insert. Store at 20° - 25°C (68° - 77°F). [See USP Controlled Room Temperature.] Avoid excessive heat.</p>	<p>NDC 70069-221-01</p> <p><b>Isosulfan Blue Injection, 1%</b></p> <p><b>50 mg /5 mL (10 mg / mL)</b></p> <p>For Subcutaneous Use Only 5 mL Single-Dose Vial</p>	<p><b>Rx Only</b></p> <p>Manufactured by: Wintac Limited Bangalore 562123 India Code No.:KR/DRUGS/KTK/28/289/97</p> <p>Manufactured for: <b>Somerset</b> Therapeutics LLC Somerset, NJ 08873 ST-ISB11/L/00</p>		<p>No Varnish Area</p>
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# Carton label



## ISOSULFAN BLUE

isosulfan blue injection, solution

### Product Information

<b>Product Type</b>	HUMAN PRESCRIPTION DRUG	<b>Item Code (Source)</b>	NDC:70069-221
<b>Route of Administration</b>	SUBCUTANEOUS		

### Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
ISOSULFAN BLUE (UNII: 39N9K8S2A4) (ISOSULFAN BLUE INNER SALT - UNII: NS6Q291771)	ISOSULFAN BLUE	10 mg in 1 mL

### Inactive Ingredients

Ingredient Name	Strength
POTASSIUM PHOSPHATE, MONOBASIC (UNII: 4J9FJ0HL51)	2.7 mg in 1 mL
SODIUM PHOSPHATE, DIBASIC, ANHYDROUS (UNII: 22ADO53M6F)	6.6 mg in 1 mL
WATER (UNII: 059QF0K00R)	

### Product Characteristics

<b>Color</b>	GREEN (Dark bluish green color solution)	<b>Score</b>	
<b>Shape</b>		<b>Size</b>	
<b>Flavor</b>		<b>Imprint Code</b>	
<b>Contains</b>			

### Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:70069-221-06	6 in 1 CARTON	07/23/2019	
1	NDC:70069-221-01	5 mL in 1 VIAL; Type 0: Not a Combination Product		

### Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA210558	07/23/2019	

**Labeler** - Somerset Therapeutics, LLC (079947873)

**Registrant** - Somerset Therapeutics, LLC (079947873)

### Establishment

Name	Address	ID/FEI	Business Operations
Wintac Limited		677236695	ANALYSIS(70069-221) , LABEL(70069-221) , MANUFACTURE(70069-221) , PACK(70069-221)

Revised: 7/2019

Somerset Therapeutics, LLC