ICG- indocyanine green and water
KARL STORZ Endoscopy-America, Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ICG for Injection Set safely and effectively. See full prescribing information for Indocyanine Green for Injection, USP.

Initial U.S. Approval: 1959

INDICATIONS AND USAGE

ICG for Injection Set, a tricarbocyanine dye, is indicated for use with the KARL STORZ ICG Imaging System to provide real-time endoscopic visible and near-infrared fluorescence imaging. ICG for Injection Set used in conjunction with the KARL STORZ ICG Imaging System enables surgeons to perform minimally invasive surgery using standard endoscopic visible light as well as:

- Visual assessment of vessels, blood flow and related tissue perfusion. (1.1)
- Visual assessment of at least one of the major extra-hepatic bile ducts (cystic duct, common bile duct and common hepatic duct), using near-infrared imaging. Fluorescence imaging of biliary ducts with the KARL STORZ ICG Imaging System is intended for use with standard of care white light and, when indicated, intraoperative cholangiography. The device is not intended for standalone use for biliary duct visualization. (1.2)

DOSAGE AND ADMINISTRATION

Perfusion Assessment (2.1)
Under sterile conditions, reconstitute one (1) 25 mg vial of Indocyanine Green for Injection, USP using one (1) 10 mL Sterile Water for Injection, USP vial located in the ICG for Injection Set. Shake the ICG vial gently to dissolve. After reconstitution, a 25 mg vial of ICG contains 2.5 mg of dye per mL of solution, so a 1.0 mL injection contains a 2.5 mg dose of ICG. ICG must be used within 6 hours after reconstitution.
A 3 mL (7.5 mg) dose, followed by a 10 mL bolus of saline, is recommended. Multiple doses can be administered as required.
Extra-Hepatic Biliary Anatomy (2.2)
Under sterile conditions, reconstitute one (1) 25 mg vial of Indocyanine Green for Injection, USP using one (1) 10 mL Sterile Water for Injection, USP vial located in the ICG for Injection Set. Shake the ICG vial gently to dissolve. After reconstitution, a 25 mg vial of ICG contains 2.5 mg of dye per mL of solution, so a 1.0 mL injection contains a 2.5 mg dose of ICG. ICG must be used within 6 hours after reconstitution.
A 0.02 mL/kg dose that is scaled to the patient's weight, followed by a 10 mL bolus of saline, is recommended. This provides 0.05 mg/kg of ICG.

DOSAGE FORMS AND STRENGTHS

Indocyanine Green for Injection, USP is a sterile, lyophilized green powder containing 25 mg of indocyanine green with no more than 5% sodium iodide. (3)

CONTRAINDICATIONS

Indocyanine Green for Injection, USP contains sodium iodide and should be used with caution in patients who have a history of allergy to iodides because of the risk of anaphylaxis. (4)

WARNINGS AND PRECAUTIONS

- Deaths due to anaphylaxis have been reported following Indocyanine Green for Injection, USP administration during cardiac catheterization. (5.1)
- Indocyanine Green for Injection, USP is unstable in aqueous solution and must be used within 6 hours. (5.2)
- Radioactive iodine uptake studies should not be performed for at least a week following the use of Indocyanine Green for Injection, USP. (5.3)

ADVERSE REACTIONS

Most common adverse reactions are anaphylactic or urticarial reactions. These have been reported in patients with and without a history of allergy to iodides. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Diagnostic Green LLC at 1-844-424-3784 (1-844-ICG-DRUG) or e-mail: drugsafety@diagnosticgreen.com; or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Products containing sodium bisulfite reduce the absorption peak of Indocyanine Green for Injection, USP in blood. (7)

Revised: 6/2016

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

ICG for Injection Set, a tricarbocyanine dye, is indicated for use with the KARL STORZ ICG Imaging System to provide real-time endoscopic visible and near-infrared fluorescence imaging. Indocyanine Green for Injection, USP used in conjunction with the KARL STORZ ICG Imaging System enables surgeons to perform minimally invasive surgery using standard endoscopic visible light as well as:

1.1 Visual assessment of vessels, blood flow and related tissue perfusion

1.2 Visual assessment of at least one of the major extra-hepatic bile ducts (cystic duct, common bile duct and common hepatic duct), using near-infrared imaging.

Visual assessment of at least one of the major extra-hepatic bile ducts (cystic duct, common bile duct and common hepatic duct), using near-infrared imaging. Fluorescence imaging of biliary

ducts with the KARL STORZ ICG Imaging System is intended for use with standard of care white light and, when indicated, intraoperative cholangiography. The device is not intended for standalone use for biliary duct visualization.

2 DOSAGE AND ADMINISTRATION

2.1 Perfusion Assessment

Preparation of ICG for Administration

Under sterile conditions, reconstitute one (1) 25 mg vial of Indocyanine Green for Injection, USP using one (1) 10 mL Sterile Water for Injection, USP vial located in the ICG for Injection Set. Shake the ICG vial gently to dissolve. After reconstitution, a 25 mg vial of ICG contains 2.5 mg of dye per mL of solution, so a 1.0 mL injection contains a 2.5 mg dose of ICG.

Indocyanine Green for Injection, USP must be used within 6 hours after reconstitution. If a precipitate is present, discard the solution.

Dosage

A 3 mL (7.5 mg) dose followed by a 10 mL bolus of saline is recommended. Multiple doses can be administered as required, up to the maximum recommended dose.

Maximum recommended dose

The total dose of dye injected should be kept below 2 mg/kg.

Timing of ICG Administration

ICG fluorescence is quickly visible within blood vessels, tissue and organs, and it does not last very long (refer to Table 1 below).

Table 1: ICG fluorescence visibility after intravenous injection

	Blood Vessels	Organs (Kidney, Liver, Adrenal Gland, Small Bowel)
See within:	5-30 seconds	1-2 minutes
Visibility lasts:	20-30 seconds	20-120 minutes

For fluorescence imaging of PERFUSION in blood vessels, administration of the ICG should be performed at the time fluorescence imaging is requested by the physician. Multiple imaging sequences may be performed as necessary [up to the maximum dose (2 mg/kg of patient body weight)], so it is recommended to withdraw the desired dosage of ICG solution for each planned imaging sequence into separate syringes ahead of time.

Method of Administration

ICG administration is to be performed via a central or peripheral venous line. Inject the prepared dose of ICG solution into the central or peripheral line as a tight bolus and immediately followed by a bolus of 10-12 mL of normal saline for injection.

2.2 Extra-Hepatic Biliary Anatomy

Preparation of ICG for Administration

Under sterile conditions, reconstitute one (1) 25 mg vial of Indocyanine Green for Injection, USP using one (1) 10 mL Sterile Water for Injection, USP vial located in the ICG for Injection Set. Shake the ICG vial gently to dissolve. After reconstitution, a 25 mg vial of ICG contains 2.5 mg of dye per mL of solution, so a 1.0 mL injection contains a 2.5 mg dose of ICG.

Indocyanine Green for Injection, USP must be used within 6 hours after reconstitution. If a precipitate is present, discard the solution.

Dosage

A 0.02 mL/kg dose that is scaled to the patient's weight is recommended. This provides 0.05 mg/kg of ICG.

Maximum recommended dose

The total dose of dye injected should be kept below 2 mg/kg.

Timing of ICG Administration

Following intravenous injection, ICG is rapidly bound to plasma protein, of which albumin is the principle carrier (95%). ICG is taken up from the plasma almost exclusively by the hepatic parenchymal cells and is secreted entirely into the bile. For optimal fluorescence imaging of Extra-Hepatic Biliary Anatomy, ICG should be administered at least 45 minutes prior to the time fluorescence imaging is desired by the physician. If this preoperative administration is not performed, however, ICG can be administered once the patient is in the OR, as adequate fluorescence imaging is possible in as little as 15 minutes after IV injection.

Method of Administration

ICG administration is to be performed via a central or peripheral venous line. Inject the prepared weight-scaled dose of ICG solution into the central or peripheral line as a tight bolus and immediately followed by a bolus of 10-12 mL of normal saline for injection.

3 DOSAGE FORMS AND STRENGTHS

Indocyanine Green for Injection, USP is a sterile, lyophilized green powder containing 25 mg of indocyanine green with no more than 5% sodium iodide.

4 CONTRAINDICATIONS

Indocyanine Green for Injection, USP contains sodium iodide and should be used with caution in patients who have a history of allergy to iodides because of the risk of anaphylaxis.

5 WARNINGS AND PRECAUTIONS

5.1 Anaphylaxis

Deaths from anaphylaxis have been reported following Indocyanine Green for Injection, USP administration during cardiac catheterization.

5.2 Drug Instability

Indocyanine Green for Injection, USP is unstable in aqueous solution and must be used within 6 hours. However, the dye is stable in plasma and whole blood so that samples obtained in discontinuous sampling techniques may be read hours later. Sterile techniques should be used in handling the dye solution as well as in the performance of the procedures. If a precipitate is present, discard the solution.

5.3 Drug/Laboratory Test Interactions

Radioactive iodine uptake studies should not be performed for at least a week following the use of Indocyanine Green for Injection, USP.

6 ADVERSE REACTIONS

Anaphylactic or urticarial reactions have been reported in patients with or without history of allergy to iodides. If such reactions occur, treat with the appropriate agents, e.g., epinephrine, antihistamines, and corticosteroids.

7 DRUG INTERACTIONS

Preparations containing sodium bisulfite, including some heparin products reduce the absorption peak of Indocyanine Green for Injection, USP in blood and, therefore, should not be used as an anticoagulant for the collection of samples for analysis.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Animal reproduction studies have not been conducted with Indocyanine Green for Injection, USP. It is also not known whether Indocyanine Green for Injection, USP can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Indocyanine Green for Injection, USP should be given to a pregnant woman only if clearly indicated.

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 Indocyanine Green for Injection, USP is administered to a nursing woman.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have been established.

8.5 Geriatric Use

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

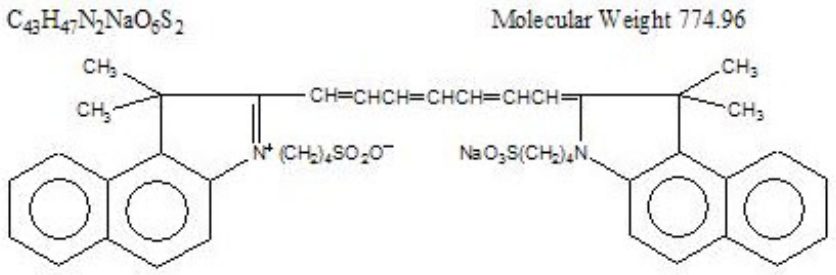
10 OVERDOSAGE

There are no data available describing the signs, symptoms, or laboratory findings accompanying overdosage. The LD_{50} after intravenous administration ranges between 60 and 80 mg/kg in mice, 50 and 70 mg/kg in rats and 50 and 80 mg/kg in rabbits.

11 DESCRIPTION

Indocyanine Green for Injection, USP is a sterile, lyophilized green powder containing 25 mg of indocyanine green with no more than 5% sodium iodide. It is packaged with Sterile Water for Injection, USP used to dissolve the indocyanine green. Indocyanine Green for Injection, USP is to be administered intravenously.

Indocyanine green is a water soluble, tricarbocyanine dye with a peak spectral absorption at 800 nm. The chemical name for Indocyanine Green is 1 *H*-Benz[*e*]indolium, 2-[7-[1,3-dihydro-1,1-dimethyl-3-(4-sulfobutyl)-2*H*-benz[*e*] indol-2-ylidene]-1,3,5-heptatrienyl]-1,1-dimethyl-3-(4-sulfobutyl)-,hydroxide, inner salt, sodium salt. Indocyanine Green for Injection, USP has a pH of approximately 6.5 when reconstituted. Each vial of Indocyanine Green for Injection, USP contains 25 mg of indocyanine green as a sterile lyophilized powder.



12 CLINICAL PHARMACOLOGY

Following intravenous injection, Indocyanine Green for Injection, USP is rapidly bound to plasma protein, of which albumin is the principle carrier (95%). Indocyanine Green for Injection, USP undergoes no significant extrahepatic or enterohepatic circulation; simultaneous arterial and venous blood estimations have shown negligible renal, peripheral, lung or cerebro-spinal uptake of the dye. Indocyanine Green for Injection, USP is taken up from the plasma almost exclusively by the hepatic parenchymal cells and is secreted entirely into the bile.

The peak absorption and emission of Indocyanine Green for Injection, USP lie in a region (800 to 850 nm) where transmission of energy by the pigment epithelium is more efficient than in the region of visible light energy. Indocyanine Green for Injection, USP also has the property of being nearly 98% bound to blood protein.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No studies have been performed to evaluate the carcinogenicity, mutagenicity, or impairment of fertility.

16 HOW SUPPLIED/STORAGE AND HANDLING

ICG for Injection Set is a kit (NDC 70599-424-02) containing one Indocyanine Green for Injection, USP kit (NDC 70100-424-02) and these Instructions For Use with the KARL STORZ ICG Imaging System.

The Indocyanine Green for Injection, USP kit (NDC 70100-424-02) contains six 25 mg Indocyanine Green for Injection, USP vials and six 10 mL Sterile Water for Injection, USP plastic vials:

NDC 70100-424-01 Indocyanine Green for Injection, USP vial. 25 mg fill in 25 mL vial.

NDC 63323-185-10 (or NDC 0409-4887-17) Sterile Water for Injection, USP, 10 mL fill in 10 mL plastic vials.

ICG for Injection Set

Distributed by:

KARL STORZ Endoscopy-America, Inc.
El Segundo, CA 90245 USA

50441

PRINCIPAL DISPLAY PANEL - KIT CARTON

Front Panel

Back Panel

Left Panel

Right Panel

Kit Carton Label

Front Panel

NDC 70599-424-02 PN: VTG0001

ICG for Injection Set

For Intravenous Administration 25 mg/Vial Kit Rx Only - Sterile

STORZ
KARL STORZ-ENDOSKOPE

Back Panel

NDC 70599-424-02 PN: VTG0001

ICG for Injection Set

Contents:
Six Indocyanine Green for Injection, USP vials (25 mg each)
Six Sterile Water for Injection, USP Vials (10 mL each)

Lot Code Area
No Print / No Coating

STORZ
KARL STORZ-ENDOSKOPE

For Intravenous Administration 25 mg/Vial Kit Rx Only - Sterile 06/2016

Left Panel

ICG for Injection Set

DIRECTIONS FOR USE ENCLOSED

CAUTION: To ensure accurate readings,
Indocyanine Green, USP dissolved in Sterile Water
for Injection, USP must be used within 6 hours.

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

USAGE: See package insert for dosage information.

25 mg/Vial Kit

Right Panel

ICG for Injection Set

Distributed by:
KARL STORZ
Endoscopy-America, Inc.
2151 E. Grand Ave.
El Segundo, CA 90245
Phone: (800) 421-0837
Fax: (800) 321-1304
E-Mail: communications@karlstorz.com
Web: www.karlstorz.com

Rx Only

25 mg/Vial Kit

PRINCIPAL DISPLAY PANEL - VIAL

Vial Label

NDC 70100-424-01

Indocyanine Green
for Injection, USP

25 mg/Vial

For Intravenous Administration
After reconstitution, use within 6 hours.

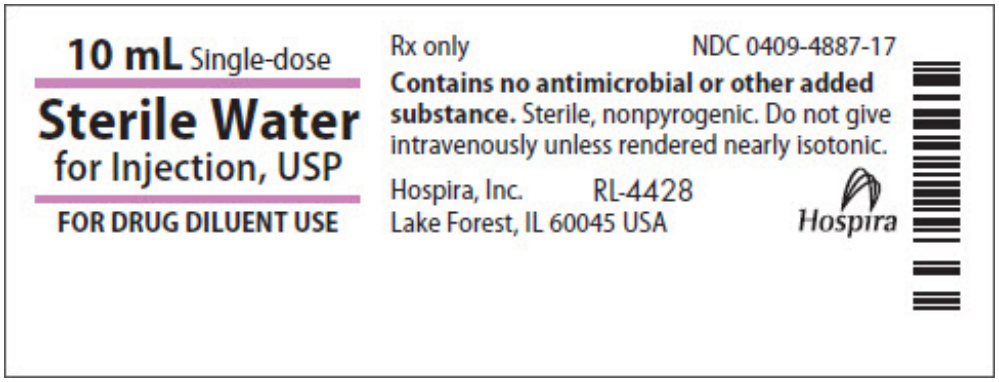
Rx only Sterile

Distributed by Diagnostic Green LLC

50428

Lot. No.
Exp.

PRINCIPAL DISPLAY PANEL - STERILE WATER VIAL



Sterile Water Label

10 mL Single-dose

Sterile Water
for Injection, USP

FOR DRUG DILUENT USE

Rx only NDC 0409-4887-17

Contains no antimicrobial or other added substance. Sterile, nonpyrogenic. Do not give intravenously unless rendered nearly isotonic.

Hospira, Inc. RL-4428
Lake Forest, IL 60045 USA

ICG

indocyanine green and water kit

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:70599-424

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:70599-424-02	6 in 1 CARTON	06/01/2016	06/01/2020
1		1 in 1 PACKAGE; Type 0: Not a Combination Product		

Quantity of Parts		
Part #	**Package Quantity**	**Total Product Quantity**
Part 1	1 VIAL	1
Part 2	1 VIAL, PLASTIC	10 mL

Part 1 of 2

INDOCYANINE GREEN

indocyanine green injection, powder, lyophilized, for solution

Product Information	
Route of Administration	INTRAVENOUS

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
INDOCYANINE GREEN (UNII: IX6J1063HV) (INDOCYANINE GREEN ACID FORM - UNII:C4V974V932)	INDOCYANINE GREEN	25 mg

Inactive Ingredients	
Ingredient Name	**Strength**
SODIUM IODIDE (UNII: F5WR8N145C)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1		1 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	ANDA040811	01/01/2008	

Part 2 of 2

STERILE WATER

water injection

Product Information	
Item Code (Source)	NDC:0409-4887
Route of Administration	INTRAVENOUS

Active Ingredient/Active Moiety		
Ingredient Name	Basis of Strength	Strength
WATER (UNII: 059QF0KO0R) (WATER - UNII:059QF0KO0R)	WATER	1 mL in 1 mL

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0409-4887-17	10 mL in 1 VIAL, PLASTIC; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA018801	10/27/1982	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA040811	06/01/2016	

Labeler - KARL STORZ Endoscopy-America, Inc. (075293423)