INDOCYANINE GREEN- indocyanine green and water
Olympus America, Inc.

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

Indocyanine Green for Injection USP Fore Intravenous Injection
Initial U.S. Approval: 1959

INDICATIONS AND USAGE

Indocyanine Green for Injection USP a tricarbocyanine dye, is indicated:

- For visual assessment of blood vessels, blood flow and related tissue perfusion with OLYMPUS infrared compatible endoscopic imaging system (1.1)
- For visual assessment of the major extrahepatic bile ducts with OLYMPUS infrared imaging endoscopic imaging system (1.2)
- For viewing intra-operative blood flow in the cerebral area with OLYMPUS infrared compatible video microscopic imaging system (1.3)

DOSAGE AND ADMINISTRATION

For visual assessment of blood vessels, blood flow and related tissue perfusion (2.1)
Under sterile conditions, the Indocyanine Green for Injection USP powder should be dissolved with the 10 mL Sterile Water for Injection, USP provided and the solution used within 6 hours after it is prepared. The usual doses of Indocyanine Green for Injection USP is 0.1 mg/kg (0.04 mL/kg) – 0.3 mg/kg (0.12 mL/kg). Immediately follow each ICG intravenous injection with a tight bolus injection of approximately 10 - 12 mL of normal saline immediately before IR imaging. Multiple administrations can be performed, up to 2 mg/kg (0.8 mL/kg) per patient.
For visual assessment of the major extrahepatic bile ducts (2.2)
Under sterile conditions, the Indocyanine Green for Injection USP powder should be dissolved with the 10 mL Sterile Water for Injection, USP provided and the solution used within 6 hours after it is prepared. The usual doses of Indocyanine Green for Injection USP is 3.0 mg (1.2 mL). Immediately follow each ICG intravenous injection with a tight bolus injection of approximately 10 - 12 mL of normal saline at least 30 minutes prior to IR imaging. Multiple administrations can be performed, up to 2 mg/kg (0.8 mL/kg) per patient.
For viewing intra-operative blood flow in the cerebral area (2.3)
Under sterile conditions, the Indocyanine Green for Injection USP powder should be dissolved with the 10 mL Sterile Water for Injection, USP provided and the solution used within 6 hours after it is prepared. The usual doses of Indocyanine Green for Injection USP is 0.1 mg/kg (0.04 mL/kg) – 0.3 mg/kg (0.12 mL/kg). Immediately follow each ICG intravenous injection with a tight bolus injection of approximately 10 - 12 mL of normal saline immediately before IR imaging Multiple administrations can be performed, up to 2 mg/kg (0.8 mL/kg) per patient.

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: 6/2020

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Indocyanine Green for Injection USP is indicated:

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

For visual assessment of blood vessels, blood flow and related tissue perfusion with OLYMPUS infrared compatible endoscopic imaging system

1.2 Visual assessment of the major extrahepatic bile duct

For visual assessment of the major extrahepatic bile ducts with OLYMPUS infrared imaging endoscopic imaging system.

1.3 Viewing intra-operative blood flow in the cerebral area

For viewing intra-operative blood flow in the cerebral area with OLYMPUS infrared compatible video microscopic imaging system

2 DOSAGE AND ADMINISTRATION

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

Under sterile conditions, the Indocyanine Green for Injection USP powder should be dissolved with the 10 mL Sterile Water for Injection, USP provided for this product, and the solution used within 6 hours after it is prepared. If a precipitate is present, discard the solution.

The patient should be weighed and the dosage for one administration should be calculated on the basis of 0.1 mg/kg (0.04 mL/kg) - 0.3 mg/kg (0.12 mL/kg) of body weight. Multiple administrations can be performed, up to 2 mg/kg (0.8 mL/kg) per patient.

ICG should be administrated immediately before IR imaging.

Item	**Note**
Indocyanine Green for Injection, USP	25 mg vials of ICG powder
Sterile Water for Injection (for dissolving ICG)	10 mL vial of sterile water
Syringe (for injecting sterile water into the ICG vial)	Use the syringe whose minimum volume is 10 mL
Syringes (for each administration)	Considering the administration volume, select the appropriate size
Sterile normal saline (for each saline flush)	Approximately 10 – 12 mL following each ICG administration
Syringes (for each saline flush)	Use the syringe whose minimum volume is 12 mL

Prepare the syringes filled with the weight-scaled dose of ICG solution, and the syringes filled with 10 - 12 mL of normal saline for the tight bolus injection.

Immediately before IR imaging, administer the prepared dose of ICG solution intravenously. Immediately follow each ICG injection with a tight bolus injection of approximately 10 - 12 mL of normal saline.

2.2 Visual assessment of the major extrahepatic bile duct

Under sterile conditions, the Indocyanine Green for Injection USP powder should be dissolved with the 10 mL Sterile Water for Injection, USP provided for this product, and the solution used within 6 hours after it is prepared. If a precipitate is present, discard the solution.

The dosage for one administration should be 3.0 mg (1.2 mL) per patient. Multiple administration can be performed, up to 2 mg/kg (0.8 mL/kg) per patient.

ICG should be administrated at least 30 minutes prior to IR imaging.

Item	**Note**
Indocyanine Green for Injection, USP	25 mg vials of ICG powder
Sterile Water for Injection (for dissolving ICG)	10 mL vial of sterile water
Syringe (for injecting sterile water into the ICG vial)	Use the syringe whose minimum volume is 10 mL
Syringes (for each administration)	Considering the administration volume, select the appropriate size
Sterile normal saline (for each saline flush)	Approximately 10 – 12 mL following each ICG administration
Syringes (for each saline flush)	Use the syringe whose minimum volume is 12 mL

Prepare the syringes filled with 3.0 mg (1.2 mL) of ICG solution, and the syringes filled with 10 - 12 mL of normal saline for the tight bolus.

At least 30 minutes prior to IR imaging, administer the prepared dose of ICG solution intravenously. Immediately follow each ICG injection with a tight bolus injection of approximately 10 - 12 mL of normal saline.

2.3 Viewing intra-operative blood flow in the cerebral area

Under sterile conditions, the Indocyanine Green for Injection USP powder should be dissolved with the 10 mL Sterile Water for Injection, USP provided for this product, and the solution used within 6 hours after it is prepared. If a precipitate is present, discard the solution.

The patient should be weighed and the dosage for one administration should be calculated on the basis of 0.1 mg/kg (0.04 mL/kg) - 0.3 mg/kg (0.12 mL/kg) of body weight. Multiple administration can be performed, up to 2 mg/kg (0.8 mL/kg) per patient.

ICG should be administrated immediately before IR imaging.

Item	**Note**
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Prepare the syringes filled with the weight-scaled dose of ICG solution, and the syringes filled with 10 - 12 mL of normal saline for the tight bolus.

Immediately before IR imaging, administer the prepared dose of ICG solution intravenously. Immediately follow each ICG injection with a tight bolus injection of approximately 10 - 12 mL of normal saline.

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 dilution curves. 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

The safety and effectiveness of indocyanine green for visual assessment of blood vessels, blood flow and related tissue perfusion, for visual assessment of the major extrahepatic bile duct and for intra-operative blood flow in the cerebral area using this IR imaging application has not been evaluated in pediatric patients.

8.5 Geriatric Use

No overall differences in safety or effectiveness have been observed between elderly

and adult patients.

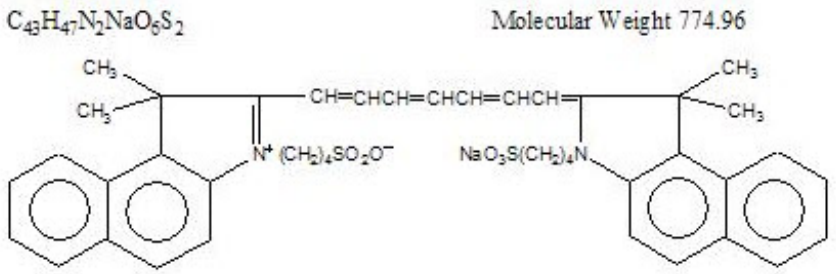
10 OVERDOSAGE

There are no data available describing the signs, symptoms, or laboratory findings accompanying overdosage. The LD50 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. Based on body surface area, these doses are 2.4 to 13-fold the maximum recommended human (MRHD) dose of 2 mg/kg for indicator-dilution studies, 10 to 52-fold the MRHD of 0.5 mg/kg for hepatic-function studies, and 7 to 39-fold the MRHD of 0.67 mg/kg for ophthalmic angiography studies.

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

Indocyanine Green for Injection USP permits recording of the indicator-dilution curves for both diagnostic and research purposes independently of fluctuations in oxygen saturation. 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. After biliary obstruction, the dye appears in the hepatic lymph, independently of the bile, suggesting that the biliary mucosa is sufficiently intact to prevent diffusion of the dye, though allowing diffusion of bilirubin. These

characteristics make Indocyanine Green for Injection USP a helpful index of hepatic function.

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, and therefore, excessive dye extravasation does not take place in the highly fenestrated choroidal vasculature. It is, therefore, useful in both absorption and fluorescence infrared angiography of the choroidal vasculature when using appropriate filters and film in a fundus camera.

The plasma fractional disappearance rate at the recommended 0.5 mg/kg dose has been reported to be significantly greater in women than in men, although there was no significant difference in the calculated value for clearance.

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

Indocyanine Green for Injection USP is supplied in a kit (NDC 73624-424-02) containing 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.

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

Manufactured by:
Patheon Italia S.p.A.
20900 Monza (MB), ITALY

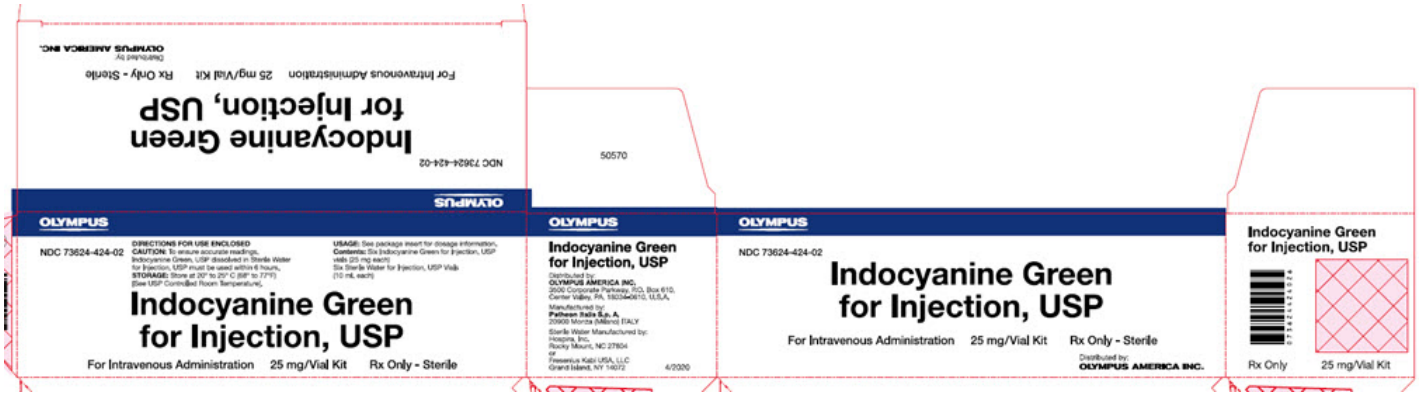
Distributed by:
OLYMPUS AMERICA INC.
3500 Corporate Parkway
P.O. Box 610
Center Valley, PA, 18034-0610

Sterile Water for Injection,
USP is manufactured by:
Fresenius Kabi USA, LLC

Grand Island, NY 14072 USA
or
Hospira, Inc.
Rocky Mount, NC 27804 USA

50652
06/2020

PRINCIPAL DISPLAY PANEL - Carton Label



Carton Label

NDC 73624-424-02

Indocyanine Green
for Injection, USP

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

Distributed by:
OLYMPUS AMERICA INC.

Back Panel

NDC 73624-424-02

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

Indocyanine Green
for Injection, USP

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

Right Panel

Indocyanine Green
for Injection, USP

Distributed by:
OLYMPUS AMERICA INC.
3500 Corporate Parkway, P.O. Box 610,
Center Valley, PA 1834-0610, U.S.A.

Manufactured by:
Patheon Italia S.p.A.
20900 Monza (Milano) ITALY

Sterile Water Manufactured by:
Hospira, Inc.
Rocky Mount, NC 27804
or
Fresenius Kabi USA, LLC
Grand Island, NY 14072

4/2020

PRINCIPAL DISPLAY PANEL - Vial Label

Vial Label

NDC 70100-424-01

Indocyanine Green
for Injection, USP

25 mg/Vial

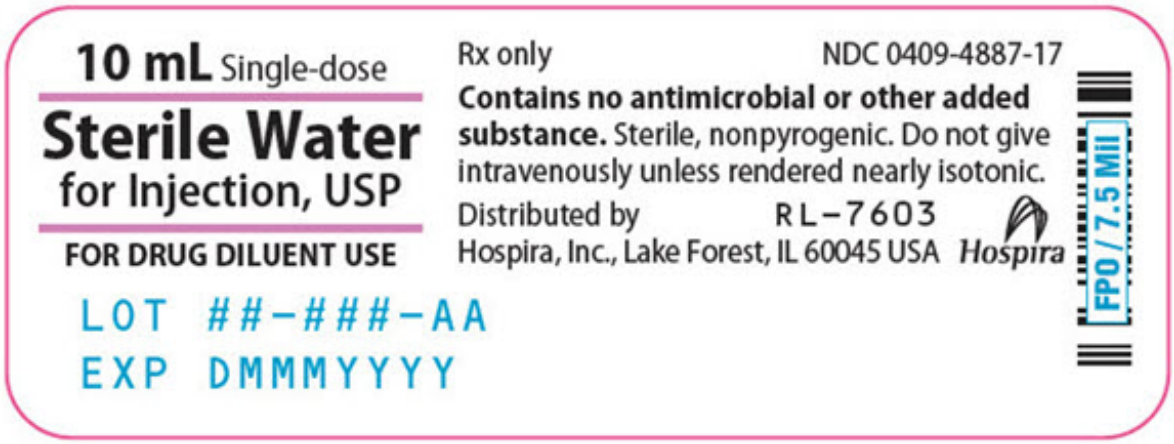
For Intravenous Administration
After reconstitution, use within 6 hours.

Rx only **Sterile**

Distributed by: Diagnostic Green LLC

50428
06/2017

PRINCIPAL DISPLAY PANEL - STERILE WATER VIAL



Sterile Water Label

10 mL Single-dose

Sterile Water
for Injection, USP

FOR DRUG DILUENT USE

LOT ##-###-AA
EXP DMMMYYYY

Rx only NDC 0409-4887-17

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

Distributed by RL-7603
Hospira, Inc., Lake Forest, IL 60045 USA

INDOCYANINE GREEN

indocyanine green and water kit

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:73624-424

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:73624-424-02	6 in 1 CARTON	04/01/2021	
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	04/01/2021	

Labeler - Olympus America, Inc. (060321254)

Revised: 6/2020 Olympus America, Inc.