Xiralite® X4

Fluorescence Imaging System

Xiralite® X4 Kit

Instructions for Use

Carefully read all instructions prior to use. Observe all warnings and precautions noted throughout these instructions. The contents of the Xiralite® X4 Kit must only be used with the Xiralite® Fluorescence Imager X4. The Xiralite® Fluorescence Imager X4 and the Xiralite® X4 Kit make up the Xiralite® Fluorescence Imaging System X4.

Xiralite® X4 Kit

Indications for use

The Xiralite® X4 Kit is indicated for use with the Xiralite® Fluorescence Imager X4.

The Xiralite® Fluorescence Imaging System X4 is an imaging system used to acquire fluorescence images for the visual assessment of circulation as a method for the evaluation of tissue perfusion and related tissue microcirculation in hands.

Description of the Xiralite® X4 Kit

Each Xiralite® X4 Kit contains six (6) 25 mg vials of ICG Imaging agent vials and six (6) 10 ml vials of Sterile Water for Injection.

The contents of the Xiralite® X4 Kit must only be used with the Xiralite® Fluorescence Imager X4.

The use of the Xiralite® X4 Kit must be in accordance with the Xiralite® X4 Kit Instructions for Use or Xiralite® Fluorescence Imager X4 Operator's Manual provided with the System.

The individual contents of Xiralite® X4 Kit are for single use only.

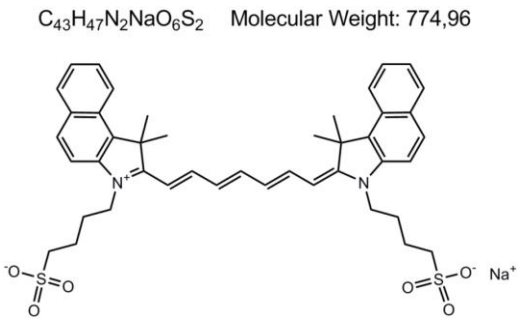
Do **NOT** re-use or re-sterilize any of the individual components of the Xiralite® X4 Kit.

The Xiralite® X4 Kit and the outside of the vials are not sterile. The inner contents of each of the components of the Xiralite® X4 Kits are supplied sterile.

The Xiralite® X4 Kit should only be used by physicians or under the supervision of physicians.

ICG

Indocyanine green is a water soluble tricarbocyanine dye with a peak spectral absorption at 800nm. Note that endogenous species have low light absorption in that range. ICG contains not more than 5.0% sodium iodide.



ICG is dissolved using Sterile Water for Injection, and is to be administered intravenously. Indocyanine Green has a pH of approximately 6.5 when reconstituted.

Before injection of ICG for each patient's imaging procedure, the ICG must be reconstituted using the Sterile Water for Injection.

ICG Characteristics

Clinical pharmacology

Following intravenous injection, Indocyanine Green is rapidly bound to plasma protein, of which albumin is the principle carrier (95%). Indocyanine Green 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 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.

Drug/drug interaction studies have not been performed.

Contraindications/ Warnings/ Precautions/ Adverse Reactions

The following safety information focuses on the components of the **Xiralite® X4 Kit**. For full Xiralite® X4 System safety information, please additionally refer to the Xiralite® Fluorescence Imager X4 Operator's Manual that is provided with the System.

Contraindications

ICG contains sodium iodide and should be used with caution in patients who have a history of allergy to iodides.

The Xiralite® Fluorescence Imaging System X4 should not be used with patients who are known to be sensitive to iodides or iodinated contrast agents.

Warnings

Anaphylactic deaths have been reported following ICG administration during cardiac catheterization.

The Sterile Water for Injection provided for this product is specially prepared and should be used to dissolve ICG because there have been reports of incompatibility with some commercially available Water for Injection.

Each vial is intended for use in only one patient.

Any prepared ICG solution remaining after each Xiralite® Fluorescence Imaging System X4 imaging procedure must be discarded.

Precautions

Indocyanine Green is unstable in aqueous solution and must only be used for one patient and within 6 hours.

Sterile techniques should be used in handling the ICG imaging agent solution as well as in the performance of the Xiralite® exam.

ICG powder may cling to the vial or lump together because it is freeze-dried in the vials. This is not due to the presence of water – the moisture content is carefully controlled. The ICG is suitable for use.

The Xiralite® X4 Kit and the outside of the vials are **NOT** sterile. The contents of the vials are sterile and must be handled aseptically.

Radioactive iodine uptake studies should not be performed for at least a week following the use of ICG.

Pregnancy Category C: Animal Reproduction studies have not been conducted with ICG. It is also not known whether Indocyanine Green can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Indocyanine Green should be given to a pregnant woman only if clearly indicated.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, a caution should be exercised when Indocyanine Green is administered to a nursing woman.

Pediatric Use: Safety and effectiveness data in pediatric patients have been established.

Only use ICG at indicated doses and concentrations as defined in the Xiralite® X4 Kit Instructions for Use.

Do not use ICG vials that appear to have seals that are compromised in any way.

However, drug/drug interactions have not been studied.

Adverse reactions

Anaphylactic or urticarial reactions have been reported after use of ICG in patients with or without history of allergy to iodides. If such reactions occur, treatment with the appropriate agents (e.g., epinephrine, antihistamines, and corticosteroids) should be administered. Resuscitative measures may also be required.

Handling, preparation and dosage of ICG

Supplies required

One (1) vial of ICG and one (1) vial of Sterile Water for Injection are required for each patient's imaging procedure.

For each imaging sequence, a set of the following supplies are required:

- One (1) 10ml syringe for reconstituting the ICG with the Sterile Water for Injection
- One (1) 3ml or 5ml syringe
- One (1) indwelling venous cannula
- One (1) extension line with a maximum internal volume of 0.1ml

Important notes:

- Injection via a peripheral antecubital venous cannula is recommended.
- A dedicated line is not required for ICG injection.
- The ICG must be reconstituted and prepared for injection before start of the imaging procedure. It must be used within 6 hours of preparation.
- There are no known drug/drug interactions with ICG.

Dosage information

For acquiring fluorescence images for the visual assessment of circulation as a method for the evaluation of tissue perfusion and related tissue microcirculation in hands the recommended dosage is 0.1 mg/kg bodyweight of ICG.

If the image quality of the examination is not deemed to be sufficient, the examination can be repeated with an increased dose of ICG at the medical discretion of the prescribing physician.

The total dose of ICG injected should be kept to below 0.5 mg/kg bodyweight.

Preparation of ICG for administration

Prepare ICG under sterile conditions.

- Draw up the entire 10ml of Water for Injection into a 10ml syringe.
- Remove the flip-off cap on one (1) ICG vial (25mg) and inject the Water for Injection through the stopper into the ICG vial. This yields a 2.5mg/ml solution of ICG. Shake the ICG vial gently to mix.
- Mix the contents of the ICG vial thoroughly and inspect the reconstituted vial for precipitation. If precipitation is noted, continue to gently shake until all ICG is dissolved into solution.

  If a precipitate is present, do **NOT** use the mixture. Discard the reconstituted vial and prepare a new vial, as described above.
- Calculate the desired ICG dose depending on body weight of the patient. Draw up the desired volume into a 3ml or 5ml syringe.
- Connect the syringe to the extension line with a maximum internal volume of 0.1ml and remove the air by carfully filling the line with ICG solution.
- Connect the free end of the filled extension line to the venous cannula, which must already be placed into an antecubital vein. **DO NOT INJECT AT THIS TIME**.

Saline Flush Preparation

Using an extension line with a maximum internal volume of 0.1 ml allows that the needed dose of ICG can be rapidly injected to ensure a bolus with a sharp wave-front. With the small internal volume of the extension line there is no need for an additional saline flush to achieve this bolus.

Administration via a Peripheral Venous Line

ICG administration is to be performed via a peripheral venous line inserted into an antecubital vein. Do not use a vein on the hand as this may influence the image appearance.

Optimal image quality is achieved when the injection of ICG enters the field of view as a sharp wave-front. This requires that dilution of the ICG solution be minimized prior to the bolus entering fast flowing blood. Attention to the following principle will help to optimize image quality:

- Promptly push the bolus of ICG into the blood stream by using the small volume (≤ 0.1ml) extension line. This small volume extension line ensures that the ICG is promptly delivered into the blood stream without a saline flush.

Timing of ICG administration

To assure a standardized quality of the imaging exam, the administration of ICG takes place 10 seconds after the beginning of the image acquisition. A timer on the screen of the Xiralite® fluorescence imager X4, counting backwards from 10 to 0 in a brown colour, provides the exact injection time point.

Discard any unused reconstituted ICG after the examination is complete. Only use the instructions for ICG preparation and injection outlined in this **Instructions for Use**.

How ICG is supplied

The Xiralite® X4 Kit and the outside of the vials are NOT sterile. The contents of the vials are supplied sterile and must be handled aseptically.

Each ICG vial is supplied for single patient use only. **DO NOT RE-STERILIZE. DO NOT RE-USE.**

Each vial of ICG should be reconstituted with an entire single 10 ml vial of Sterile Water for Injection just prior to the imaging procedure(s). Any prepared ICG solution remaining at the end of a procedure must be discarded.

Storage of ICG

The Xiralite® X4 Kit should be stored at ambient room temperatures of 20° to 25°C (68° to 77°F).

Technical support and supplies

To order additional supplies or for technical information contact mivenion GmbH at +49 30 68837920 or at sales@mivenion.com.

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