▼ This medicinal product is subject to additional monitoring **in Australia**. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/safety/reporting-problems

AUSTRALIAN PRODUCT INFORMATION

SPY AGENT GREEN (INDOCYANINE GREEN)

1 NAME OF THE MEDICINE

Indocyanine green

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

SPY AGENT GREEN is presented as a sterile lyophilised green powder containing 25mg of indocyanine green as the active ingredient in a 20 mL vial, which contains no more than 5% sodium iodide.

For the full list of excipients, see section **6.1 List of excipients**.

3 PHARMACEUTICAL FORM

Powder for injection.

SPY AGENT GREEN is presented as a sterile lyophilised green powder containing 25 mg of indocyanine green in a 20 mL vial.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

For fluorescence imaging use only.

SPY AGENT GREEN (indocyanine green) is an imaging agent (dye) intended for:

1. Visualisation of vessels, blood flow and tissue perfusion in adults and paediatric patients from one month of age and above.
2. Visualisation of extrahepatic biliary ducts in adults and children from 12 years of age and above.
3. Visualisation of lymph nodes and lymphatic vessels in women with cervical or uterine solid tumours for which lymphatic mapping is a component of intraoperative management.

Visualisation with SPY AGENT GREEN requires an imaging system that has been validated for fluorescence imaging with indocyanine green

Please see 5.1 PHARMACODYNAMIC PROPERTIES – Clinical Trials

4.2 DOSE AND METHOD OF ADMINISTRATION

SPY AGENT GREEN is for intravenous and interstitial administration according to the indication.

Refer further below the relevant "**Dose and Method of Administration**" and the **Reconstitution Instructions**.

Visualisation of Vessels, Blood Flow and Tissue Perfusion

Dose and Method of Administration

Adults:

The recommended dose of SPY AGENT GREEN for a single image sequence is 1.25 mg to 5 mg of a 2.5 mg/mL solution.

For visualisation of perfusion in extremities through the skin, the recommended dose is 3.75 mg to 10 mg of a 2.5 mg/mL solution.

Immediately flush with a 10 mL bolus of 0.9% Sodium Chloride.

Paediatric population:

The recommended dose for a single image sequence is 1.25 mg to 5 mg SPY AGENT GREEN of a 2.5 mg/mL solution. Lower doses may be administered in younger patients and in those with lower body weight. Immediately flush with bolus. Adjust the amount and type of flush to avoid volume and/or sodium overload.

Additional doses may be administered to obtain imaging sequences during the procedure. Do not exceed the maximum total dose of 2 mg/kg.

Prior to the imaging procedure, draw up the desired dosage of SPY AGENT GREEN solution into appropriate syringes and prepare a 10 mL syringe of 0.9% Sodium Chloride.

Administer via a central or peripheral venous line using a three-way stopcock attached to an injection port on the infusion line.

Inject the prepared SPY AGENT GREEN into the line as a tight bolus. Immediately switch the access on the stopcock and inject the prepared flush.

Imaging Instructions for Visualisation of Vessels, Blood Flow and Tissue Perfusion
SPY AGENT GREEN may be used with an imaging system that is intended for fluorescence imaging with indocyanine green.

A fluorescence response should be visible in blood vessels within 5 to 15 seconds after injection.

Visualisation of Extrahepatic Biliary Ducts

Dose and Method of Administration

The recommended single dose of SPY AGENT GREEN for adults and paediatric patients aged 12 years of age and above is 2.5 mg of a 2.5 mg/mL solution administered intravenously as a single dose at least 45 minutes prior to surgery. Additional doses may be administered to obtain imaging sequences during the procedure.

Do not exceed a total dose of 2 mg/kg.

Imaging Instructions for Visualisation of Extrahepatic Biliary Ducts

SPY AGENT GREEN may be used with an imaging system that is intended for fluorescence imaging with indocyanine green. Fluorescence is visible in the biliary tree within 45 minutes after injection.

Visualisation of Lymph Nodes and Lymphatic Vessels During Lymphatic Mapping for Cervical and Uterine Tumours

Dose and Method of Administration

The recommended single dose of SPY AGENT GREEN is 5 mg of a 1.25 mg/mL solution [four 1 mL injections administered interstitially into the cervix, at the three o' clock and the nine o'clock positions with a superficial (1 mm to 3 mm) and a deep (1 cm to 3 cm) injection at each position].

Imaging Instructions for Visualisation of Lymph Nodes and Lymphatic Vessels During Lymphatic Mapping

SPY AGENT GREEN may be used with an imaging system that is intended for fluorescence imaging with indocyanine green.
Fluorescent lymphatic vessels and lymph nodes should begin to be visible within 1 minute after injection.

Reconstitution Instructions

Prepare SPY AGENT GREEN under sterile conditions prior to surgery. SPY AGENT GREEN is reconstituted with 10 mL or 20 mL of sterile Water for Injections prior to use to form a 2.5 mg/mL or 1.25 mg/mL solution of indocyanine green. The reconstitution volume is dictated by the type of imaging to be undertaken. Refer below for further instructions.

Inspect the reconstituted solution for particulate matter. The reconstituted solution should be a clear, green solution. If precipitation is noted, continue to gently swirl the vial until SPY AGENT GREEN is dissolved. If precipitation persists, discard and prepare a new vial.

Visualisation of Vessels, Blood Flow, and Tissue Perfusion and Visualisation of Extrahepatic Biliary Ducts

Dissolve SPY AGENT GREEN with 10 mL Sterile Water for Injections to form a concentration of 2.5 mg indocyanine green/mL.

Visualisation of Lymph Nodes and Lymphatic Vessels During Lymphatic Mapping

Dissolve SPY AGENT GREEN with 20 mL Sterile Water for Injections to form a concentration of 1.25 mg indocyanine green/mL.

4.3 Contraindication

SPY AGENT GREEN is contraindicated in patients with a history of hypersensitivity to indocyanine green or any of excipients [see **6.1 List of excipients**]. Reactions have included anaphylaxis [see **4.4 Special warnings and precautions for use**].

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Hypersensitivity Reactions

Hypersensitivity reactions including anaphylaxis, urticaria, and deaths due to anaphylaxis have been reported following intravenous administration of indocyanine green. [see **4.8 Adverse effects (Undesirable effects)**]. Always have cardiopulmonary resuscitation personnel and equipment readily available and monitor all patients for hypersensitivity reactions.

Interference with Radioactive Iodine Uptake Studies

Because SPY AGENT GREEN contains iodine, the iodine-binding capacity of thyroid tissue may be reduced for at least one week following administration. Do not perform radioactive iodine uptake studies for at least a week following administration of SPY AGENT GREEN [see **4.5 Interactions with other medicines and other forms of interaction**].

Use in the elderly

Of the total number of subjects in clinical studies of SPY AGENT GREEN in visualisation of vessels, blood flow, and tissue perfusion, 7 percent were 65 and over, while 1 percent were 75 and over and of the total number of subjects in clinical studies of SPY AGENT GREEN in visualisation of lymph nodes and lymphatic vessels during lymphatic mapping, 9 percent were 65 and over, while 2 percent were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Clinical studies of SPY AGENT GREEN in visualisation of extrahepatic biliary ducts did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Paediatric use

Use of indocyanine green for visualisation of vessels, blood flow and tissue perfusion has been established in paediatric patients one month and older. Paediatric use is supported by published data in 49 paediatric patients who received indocyanine green for assessment of blood flow and tissue perfusion in cardiovascular, vascular and plastic, micro and reconstructive procedures, and by clinical trials in adults. No overall differences in safety or effectiveness have been observed between paediatric patients and adults. The dose range was similar to the effective dose range in adults [See **4.2 Dose and method of administration**]. The use of indocyanine green for visualisation of vessels, blood flow and tissue perfusion has not been established in paediatric patients less than one month of age.

Use of indocyanine green for visualisation of extrahepatic biliary ducts has been established in

paediatric patients aged 12 and above. Paediatric use is supported by clinical trials in adults in addition to clinical use in paediatric patients. No overall differences in safety or effectiveness have been observed between paediatric patients and adults. The dose range was similar to the effective dose range in adults [See **4.2 Dose and method of administration**]. The use of Indocyanine green for visualisation of extrahepatic biliary ducts has not been established in paediatric patients less 12 years of age.

The safety and efficacy of indocyanine green for visualisation of lymph nodes and lymphatic vessels during lymphatic mapping for cervical and uterine tumours has not been established in paediatric patients.

Effects on laboratory tests

Not applicable.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

No specific interactions of indocyanine green with other medicinal products are known.

Effect on Radioactive Iodine Uptake Studies

Because SPY AGENT GREEN contains iodine, the iodine-binding capacity of thyroid tissue may be reduced for at least one week following administration. Do not perform radioactive iodine uptake studies for at least one week following administration of SPY AGENT GREEN [see **4.4 Special warnings and precautions for use**].

Paediatric population:
No specific interactions of indocyanine green with other medicinal products are known.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No studies examining the effects of SPY AGENT GREEN on fertility have been conducted.

Use in pregnancy – Pregnancy Category B2

There are no adequate and well-controlled studies of SPY AGENT GREEN in pregnant women. Available data from a very small number of scientific literature studies with indocyanine green use in pregnant women over several decades have not reported any drug associated risks for major birth defects, miscarriage, or adverse maternal or foetal outcomes. Data from one small study in which indocyanine green was administered intravenously to pregnant women during labour suggest there is no placental transfer of the drug. Animal reproduction studies have not been conducted with indocyanine green.
SPY AGENT GREEN should be given to a pregnant woman only if clearly indicated.

Use in lactation

Seventeen cases of indocyanine green use in lactating women have been reported in the scientific literature with no adverse events observed in the breastfed infant. However, there are no data on the presence of indocyanine green in human milk or the effects on milk production. Therefore, the developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for SPY AGENT GREEN and any potential adverse effects on the breastfed infant from SPY AGENT GREEN or from the underlying maternal condition.

No post-natal developmental studies in animals were conducted with indocyanine green.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No effects on the ability to drive and use machinery have been observed.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The following adverse reactions are discussed in greater detail in other sections of the Data Sheet:

- Hypersensitivity Reactions [see **4.4 Special warnings and precautions for use**].

The following adverse reactions have been identified during post-approval use of Indocyanine green. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Immune System Disorders: Anaphylaxis, urticaria.

Reporting suspected adverse effects
Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

There are no data available describing the signs, symptoms, or laboratory findings accompanying overdose.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

There is no relevant pharmacodynamic data.

Mechanism of action

When bound to proteins in plasma or in lymph fluid, indocyanine green absorbs light in the near-infrared region at 805 nm, and emits fluorescence (light) at a slightly longer wavelength, with peak emission at 830 nm. Fluorescence imaging devices provide external energy as near

infrared light for ICG to absorb, resulting in excitation of the ICG and the emitted light (fluorescence) is transferred from the field of view to an image on a monitor. These optical properties of indocyanine green are utilised in fluorescence imaging of the micro and macro vasculature, blood flow and tissue perfusion, the extrahepatic biliary ducts, and for lymphatic mapping of lymph nodes and lymphatic vessels.

Clinical trials

Trial Design and Study Demographics

The efficacy and safety of SPY AGENT GREEN (indocyanine green for injection) was assessed in one open-label, controlled, multicentre, single arm, within patient, lymphatic mapping study in patients with uterine and cervical cancer (FILM study) and in four (4) systematic summary reviews, in the form of meta analyses, of published literature with use of indocyanine green as the imaging agent for Novadaq Fluorescence Imaging Systems and the da Vinci Surgical Robotic System. The four (4) meta-analysis included one in lymphatic mapping in patients with uterine and cervical cancer (Study LNM-UC01), and three related systematic summary reviews, one for visualisation of macrovascular blood flow, one for visualisation of microvascular tissue perfusion and one for visualisation of extrahepatic biliary anatomy (Studies Macro-IAM-01, Micro-IAM-01 and Biliary-IAM-01, respectively).

A total of 176 patients were treated with SPY AGENT GREEN in the FILM study and further clinical experience with lymphatic mapping using indocyanine green in 1,512 patients with uterine and cervical cancer was provided from Study LNM-UC01. A follow-up systematic review of the published literature, using the same study design and methodology as Study LNM-UC01, was conducted and provided data from an additional 441 patients with uterine and cervical cancer. The results from the follow-up review were consistent with the results from Study LNM-UC01.

Data from 1,184 and 2,055 patients undergoing various surgical procedures requiring visualisation of blood flow and tissue perfusion, are provided from Studies Macro-IAM-01 and Micro-IAM-01, respectively. Clinical experience with visualisation of the main extrahepatic biliary ducts using indocyanine green and SPY Fluorescence Imaging Systems in 314 patients is provided from Study Biliary-IAM-01. Follow-up systematic reviews of the published literature, using the same study designs and methodology as Studies Macro-IAM-01, Micro-IAM-01 and Biliary-AIM-01 were conducted and provided data from an additional 292 patients undergoing procedures requiring visualisation of microscopic blood flow and 245 patients requiring visualisation of extrahepatic biliary anatomy. The results from the follow-up reviews were consistent with the results from the original Studies.

Visualisation of Vessels, Blood Flow and Tissue Perfusion

Study Macro-IAM-01

Study Macro-IAM-01 was a systematic review, in the form of a meta-analysis, of 13 studies examining the use of Novadaq fluorescence imaging systems, including the da Vinci system, for visualisation of macrovascular blood flow in vessels (i.e., arteries, veins and bypass grafts) during various procedures including, but not limited to, coronary bypass surgery, organ transplant procedures, plastic reconstructive surgery utilising autologous flaps, renal cancer and vascular surgeries. A total of 1,184 patients were evaluated in this meta-analysis. The indocyanine green was administered as a single administration pre- or intraoperatively and

may have included a repeat administration during surgery. Indocyanine green doses ranged from 0.0125 mg – 25 mg across all 13 studies. The primary endpoint was the success rate of intraoperative visualisation of macrovascular blood flow in vessels.

The results showed an overall visualisation success rate of 97.0% with 95% CI of 96.3% to 97.6%, meeting the success criteria of the study. There were a total of 2,854 visualisations attempted and 2,768 visualisations succeeded. Across the 13 studies reviewed, 12 studies exceeded the success criteria of a 90% visualisation rate and 10/13 studies showed a 100% visualisation rate.

Study Micro-IAM-01

Study Micro-IAM-01 was a systematic review, in the form of a meta-analysis, of 33 studies examining the use of Novadaq fluorescence imaging systems, including the da Vinci system, for visualisation of microvascular blood flow in tissues during various procedures including, but not limited to, myocardial perfusion in cardiac and cardiovascular surgeries, tissue flap perfusion in plastic reconstructive surgery, perfusion in vascular surgeries (such as wound, amputation and coronary vessels), GI tract perfusion during surgery of the colon, stomach or esophagus and parathyroid perfusion during endocrine surgery. A total of 2,055 patients were evaluated in this meta-analysis. The indocyanine green was administered as a single administration pre- or intraoperatively and may have included a repeat administration during surgery. Indocyanine green doses ranged from 2.5 mg – 17.5 mg across all 33 studies. The primary endpoint was the success rate of intraoperative visualisation of microvascular blood flow in tissues.

The results showed an overall visualisation success rate of visualisation success rate of 99.9% with 95% CI of 99.7% to 100.0%. All of the studies showed a success rate greater than 90% and therefore, met the study success criteria. There were a total of 2,696 visualisations attempted and 2,693 succeeded. Across the 33 studies reviewed, all of the studies exceeded the success criteria of a 90% visualisation rate and 31/33 studies showed a 100% visualisation rate.

Visualisation of Extrahepatic Biliary Ducts

Study Biliary-IAM-01

Study Biliary-IAM-01 was a systematic review, in the form of a meta-analysis, of 4 studies examining the use of Novadaq fluorescence imaging systems, including the da Vinci system, for visualisation of extrahepatic biliary anatomy. A total of 314 patients were evaluated in this meta-analysis. The indocyanine green was administered as a single administration preoperatively and may have included a repeat administration during surgery. Indocyanine green doses ranged from 1.4 mg – 17.5 mg across the 4 studies. The primary endpoint was the success rate of intraoperative visualisation of at least one of the major extrahepatic bile ducts (cystic duct, common bile duct or common hepatic duct).

The results showed an overall visualisation success rate of 99.3%, with 95% CI of 97.3% to 100.0%. There were a total of 286 visualisations attempted and 284 succeeded. All 4 studies showed a success rate greater than 90% and therefore, met the study success criteria.

Visualisation of Lymph Nodes and Lymphatic Vessels During Lymphatic Mapping of Cervical and Uterine Tumours

FILM Study

FILM was a randomised, prospective, multi-centre, open-label study in patients with early stage uterine or cervical cancers and no known regional nodal or metastatic disease by standard clinical evaluation. Indocyanine green and a blue dye comparator were injected into the cervix of patients at the beginning of the operative procedure. A total of 176 patients were randomised to receive either indocyanine green followed by blue dye or blue dye followed by indocyanine green. A total of four 1 ml injections of a 1.25 mg/ml solution of indocyanine green were administered into the cervix at the 3 and 9 o'clock positions with a superficial (1 to 3 mm) and a deep (1 to 3 cm) injection at each position for a total dose of 5 mg per patient. Lymphatic mapping was performed intraoperatively using the PINPOINT Fluorescence Imaging System and standard light, followed by excision of tissues identified by indocyanine green, blue dye, or the surgeon's visual and palpation examination. The resected tissues were evaluated by histopathology to confirm presence of lymph nodes. The efficacy of indocyanine green and the PINPOINT Fluorescence Imaging System in the detection of lymphatic vessels and lymph nodes during lymphatic mapping procedures was determined by the number of histology-confirmed lymph nodes detected by indocyanine green and/or the blue dye comparator.

Table 1 shows the distribution of resected, confirmed lymph nodes by the presence or absence of indocyanine green or blue dye in the modified intent-to-treat population (mITT). Among the confirmed lymph nodes identified, 93% were identified using indocyanine green, and 43% were identified using blue dye, a difference of 50% [95% confidence interval 39% to 60%].

Table 1: Distribution of Resected Confirmed Lymph Nodes Detected by indocyanine green (ICG) or Blue Dye (BD)

Analysis population	Nodes (n)	All Lymph nodes detected with ICG	All Lymph nodes detected with BD	Lymph nodes detected with ICG Only	Lymph nodes detected with BD Only	Lymph nodes detected with Neither
mITT	513	476/513 93%	220/513 43%	262/513 51%	6/513 1%	31/513 6%

Table 2 shows the number of patients with at least one resected, confirmed lymph node and the number of patients with at least one bilateral lymph node pair detected by indocyanine green or blue dye. With indocyanine green, approximately 97% of patients had at least one resected, confirmed lymph node detected and 73% had at least one bilateral lymph node pair detected, compared with 68% and 28%, respectively, with blue dye [p-values for each analysis <0.0001].

Table 2: Distribution of Patients with at Least one Confirmed Unilateral Lymph Node / Bilateral Pair Detected by indocyanine green (ICG) or Blue Dye (BD)

Analysis population	Patients (n)	Patients with All Lymph nodes detected with ICG	Patients with All Lymph nodes detected with BD	Patients with Lymph nodes detected with ICG Only	Patients with Lymph nodes detected with BD Only	Patients with Lymph nodes detected with Neither
mITT Unilateral*	172	167/172 97%	118/172 68%	51/172 30%	2/172 1%	3/172 3%
mITT Bilateral**		126/172 73%	49/172 28%	79/172 46%	2/172 1%	44/172 26%

*: patients with at least one resected confirmed lymph node detected unilaterally
**: patients with at least one resected confirmed lymph node detected unilaterally

Study LNM-UC01

Study LNM-UC01 was a meta-analysis of 11 published studies that examined the use of the investigational lymphatic mapping agent indocyanine green among patients undergoing surgery for uterine or cervical cancer. The 11 studies provided clinical data on 1,512 patients with approximately half of the data coming from studies that compared indocyanine green to blue dyes and half from studies designed only to assess indocyanine green lymph node detection rates. The predominance (70%) of the comparative clinical data came from published reports that cited use of the same indocyanine green dose (5 mg) and injection technique as that used in the FILM Study.

The results found an overall indocyanine green lymph node detection rate of 81% compared to a blue dye lymph node detection rate of 52% with an odds ratio of 3.83 and 95% CI of 2.82 to 5.21 ($p < 0.0001$). Lymph node detection was shown to be superior with indocyanine green compared to blue dye, with statistical success reported by the publication authors in four of the five comparative studies.

5.2 PHARMACOKINETIC PROPERTIES

Absorption and Distribution

Following intravenous injection, indocyanine green binds to plasma proteins (98%) and is largely confined to the intravascular compartment. Indocyanine green undergoes no significant extrahepatic or enterohepatic circulation; simultaneous arterial and venous blood estimations have shown negligible renal, peripheral, lung or cerebrospinal uptake of the dye. 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.

Following interstitial injection, indocyanine green is taken up by the lymphatic vessels and lymph nodes.

Metabolism

Indocyanine green is not metabolised after intravenous administration and excreted from the liver. It is transported unchanged by glutathione S-transferase (plasma clearance). It is not reabsorbed from the intestine and does not undergo enterohepatic circulation.

Excretion

Indocyanine green is taken up from the plasma almost exclusively by the hepatic parenchymal cells and is secreted entirely into the bile.

The plasma fractional disappearance rate at a 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.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No studies have been performed to evaluate the genotoxic potential of indocyanine green.

Carcinogenicity

No studies have been performed with indocyanine green to evaluate the carcinogenicity.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Sodium iodide
Sodium hydroxide (pH adjustment)
Hydrochloric acid (pH adjustment)

Water for Injections

6.2 INCOMPATIBILITIES

SPY AGENT GREEN must not be mixed with any other medicinal products, except those mentioned in **6.6 Special precautions for disposal**.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

Storage conditions after reconstitution

SPY AGENT GREEN contains no antimicrobial preservative. To reduce microbiological hazard, use reconstituted SPY AGENT GREEN as soon as practicable after preparation. If storage is necessary, hold at room temperature (Below 25°C) and use within 6 hours.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C.

Do not use after the expiry date.

Use in one patient on one occasion only.

For storage conditions after reconstitution of SPY AGENT GREEN, see **6.3 Shelf life**.

NATURE AND CONTENTS OF CONTAINER

Powder for injection, in a glass vial with a rubber stopper and aluminium seal.

Packs contain 1 vial or 6 vials.

6.5 SPECIAL PRECAUTIONS FOR DISPOSAL

SPY AGENT GREEN is for intravenous and interstitial administration.

Once a vial has been opened and the powder reconstituted (with Water for Injections), the contents must be used within 6 hours.

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

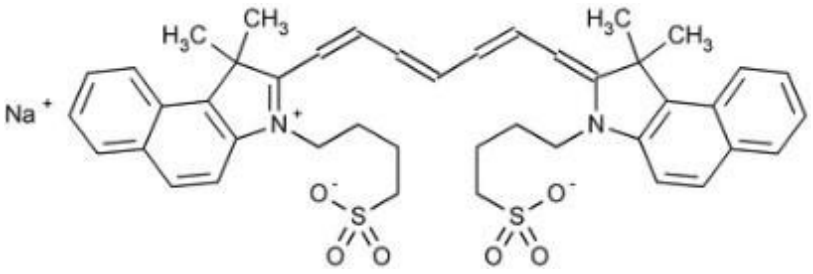
6.6 PHYSICOCHEMICAL PROPERTIES

SPY AGENT GREEN (indocyanine green for injection) is a water soluble, optical imaging agent which is reconstituted with sterile Water for Injections, for intravenous or interstitial use. Each vial contains a sterile, lyophilised green powder containing 25 mg of indocyanine green with not more than 5% sodium iodide.

Chemical structure

The chemical name for Indocyanine Green is 1 HBenz[e]indolium, 2-[7-[1,3-dihydro-1,1-dimethyl-3-(4-sulfobutyl)-2H-benz[e] indol-2-ylidene]-1,3,5-heptatrienyl]-1,1-dimethyl-3-(4-sulfobutyl)-, hydroxide, inner salt, sodium salt.

Molecular Formula: $C_{43}H_{47}N_2NaO_6S_2$; Molecular Mass: 774.96 g/mol, with the following structural formula:



Indocyanine green has a peak spectral absorption at 800 nm. SPY AGENT GREEN has a pH of 5.5 to 7.5 when reconstituted with sterile Water for Injections.

CAS number

The CAS Number is 3599-32-4.

7 MEDICINE SCHEDULE (POISONS STANDARD)

Unscheduled

8 SPONSOR

Stryker Australia Pty Ltd
8 Herbert Street
St Leonards 2065 NSW
Australia

Telephone: 1800 803 602
Email: customer.serviceau@stryker.com

9 DATE OF FIRST APPROVAL

Not yet advised

10 DATE OF REVISION

Not applicable

SUMMARY TABLE OF CHANGES

Section	Summary of new information

Changed	
	Not applicable