

Verdye (Indocyanine Green)

Minimally Invasive Surgery (MIS) Focus



Diagnostic Green is the leading provider of trusted high quality fluorescence products, for physicians worldwide

Minimally Invasive Surgery (MIS), using small incisions to minimise trauma to normal tissues and adjacent organs, is now the preferred method of undertaking many surgeries. The global minimally invasive surgical systems market is expected to grow at a CAGR of 10.9% from 2020 to 2025, driven by the rapidly increasing demand from the patients undergoing minimally invasive surgical procedures, increasing surgical need, and the surge in the prevalence of colorectal and other gastrointestinal diseases.¹ New technological advancements, such as miniaturisation of surgical equipment and development of surgical robots, have substantially increased the number of minimally invasive surgeries performed across the world.

USE OF VERDYE IN MINIMALLY INVASIVE SURGERIES INCLUDE:

Visualisation of Structures	Vascular Assessment
Laparoscopic Cholecystectomy (Lap Chole)	Laparoscopic Colectomy Oesophagectomy

Laparoscopic Cholecystectomy (Lap Chole)

Laparoscopic Cholecystectomy is the gold standard for gallbladder surgery and is one of the most common surgeries undertaken worldwide. In the USA an estimated one million Lap Chole's are undertaken each year, with an estimated 500,000 in Europe.² Whilst the incidence of Bile Duct Injury (BDI) is low at 0.5%, due to the considerable amount of surgeries, this becomes quite a significant number with thousands of resultant patients per year thus sustaining BDI's, with severe and long term implications for their health.² The primary cause of error in 97% of Lap Chole cases was a visual perception illusion, which is one of the major drawbacks of an MIS approach.³

X-Ray Cholangiography has been used in the past to overcome this visualisation problem. However it has drawbacks that are not apparent with Indocyanine Green (ICG) use.

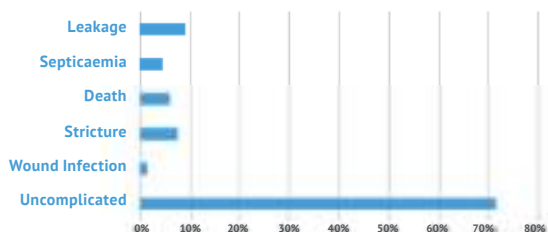
ICG Guided Cholecystectomy	X-Ray Cholangiography
Less expensive per patient vs. X-Ray cholangiography	Requires additional equipment and manpower
No radiation exposure	Involves radiation exposure
Non-invasive and less time consuming	Requires dissection of the cystic duct which takes procedure time
Highly specific (anatomy identified at a significantly higher rate) with no learning curve required	Interpretation relies on the expertise of the surgeon

Recently, a RCT demonstrated that ICG fluorescence cholangiography was equivalent to X-Ray cholangiography in its ability to visualise the critical junction (junction between the cystic duct, common hepatic duct and common bile duct).⁴ ICG fluorescence cholangiography was a faster procedure and has been shown to be a simple and cost-effective technique to recognise the biliary structures.^{4,5}

ICG fluorescence imaging during laparoscopic cholecystectomy (Lap Chole) surgery reduces BDI injuries and improves patient outcomes

THE BILE DUCT INJURY (BDI) RATE WITH LAPAROSCOPIC CHOLECYSTECTOMY IS REPORTED TO BE 0.5%², AND WHILE RELATIVELY LOW, WHEN INJURIES OCCUR, THEY CAN BE CATASTROPHIC.⁶

Outcome of Common Bile Duct Injuries following Cholecystectomy.⁴

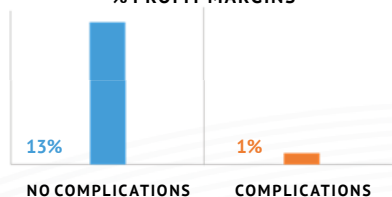


THE PRIMARY CAUSE OF ERROR IN 97% OF CASES WAS A VISUAL PERCEPTION ILLUSION.⁴



Surgeons had a 3-fold improvement in ability to visualise critical bile duct structures using ICG.⁷

LAP CHOLE HOSPITAL % PROFIT MARGINS



Profit margins at hospitals drop from 13% to 1% when complications in lap chole surgeries occur.⁸

Colorectal Surgery

Colorectal surgery frequently involves bowel resection with restoration of the alimentary tract by anastomosis. Indocyanine green (ICG) fluorescence imaging has proven to be an effective tool to assess anastomotic perfusion. Its use for the prevention of anastomotic leaks (AL) has been gaining popularity, with accumulating data on lower leak rates with (ICG) fluorescence guided surgery.^{9,12}

Most common methods used to evaluate the perfusion status of the colon has been to visually observe the change in colour of the colon wall with the surgeon's naked eye and to carefully observe the pulse of the colon wall. However, these methods are subjective and not always accurate. Reported rates of anastomotic leakage vary from 3-6% in experienced colorectal surgeons and 3-25% overall.¹⁰ Combining the use of ICG with a near-infra red (NIR) laparoscopic camera system offers the surgeon the possibility of an objective, real-time assessment of blood flow to the colon.

COMPLICATIONS VARY BY PROCEDURE

Procedure	Leak Rate	Mortality
Colon Resection	2.7%	Up to 15%
Rectal Resection	5-20%	Up to 10%
Oesophagectomy	4-25%	Up to 50%
Total/Partial Gastrectomy	5-12%	Up to 20%
Sleeve Gastrectomy	1-4%	Up to 5%



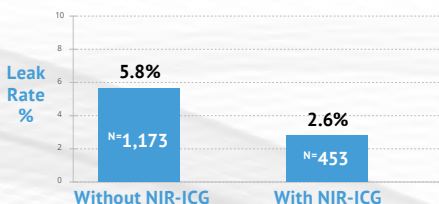
ICG PROVEN TO REDUCE LEAK RATES IN COLORECTAL SURGERY

There is a growing body of evidence that proves the significant value of using ICG in colorectal surgery. Below is a summary of two recent Clinical Trials proving that ICG is safe, effective and is increasingly viewed as the gold standard in laparoscopic colorectal procedures.

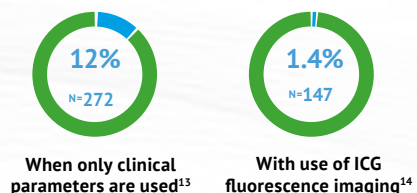
Study	Results	Study Conclusions
Multicentre phase II trial of near-infra red imaging in elective colorectal surgery. ¹¹	NIR ICG assessment change in site of bowel division 29 patients (5.8%) no subsequent leak rates in these patients. Overall Leak Rate Standard White light 5.8% versus NIR ICG 2.6% . Left Anterior Resections Standard White light 10.7% versus NIR ICG 3% .	NIR-ICG use may change intraoperative decisions, which may lead to a reduction in anastomotic leak.
Blood perfusion assessment by indocyanine green fluorescence imaging for minimally invasive rectal cancer surgery (EssentialAL trial): A randomized clinical trial. ¹²	The rate of anastomotic leakage (Grade A+B+C) was significantly lower in the ICG+ group (7.6%) than in the non-ICG group (11.8%) . The rate of anastomotic leakage (Grade B+C) was 4.7% in the ICG+ group and 8.2% in the non-ICG group .	839 patient study which showed that ICG-cohort saw that ICG-fluorescence significantly reduced the anastomotic leakage rate by 4.2% .

ICG fluorescence imaging during colorectal surgery reduces the rate of leaks experienced by patients

OVERALL LEAK RATE IN PATIENTS UNDERGOING COLORECTAL SURGERY¹¹



PATIENTS EXPERIENCING ANASTOMOTIC LEAKS FOLLOWING COLORECTAL RESECTION SURGERY



Mortality rates associated with anastomotic leaks, range from 5-17%.¹⁵
 Profit margins at hospitals drop by 8% when complications in colon surgeries occur.⁸

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VERDYE PRESCRIBING INFORMATION

Name of the Medicinal Product

Verdye 5 mg/ml Injection

25 mg / 50 mg, Powder for Solution for Injection

Pharmaceutical Form

Powder for Solution for Injection
Dark-green powder

Clinical Particulars

Therapeutic indications

This medicinal product is for diagnostic use only.

Diagnostic Indications

Cardiac, circulatory and micro-circulatory diagnostics:

- measurement of cardiac output and stroke volume
- measurement of circulating blood volumes
- measurement of cerebral perfusion

Liver function diagnostics:

- measurement of liver blood flow
- measurement of excretory function of the liver

Ophthalmic angiography diagnostics:

- measurement of perfusion of the choroid

Posology and method of administration

Method of administration

Before administration the powder must be reconstituted with water for injection.

Shelf Life

5 years. After reconstitution, the solution should be used immediately, protected from light.

Instructions for use and handling

This medicinal product should be reconstituted immediately prior to use. This medicinal product is reconstituted by addition of 5 ml water for injections to the vial containing 25 mg of active substance or 10 ml water for injections to the vial containing 50 mg of active substance, respectively, giving in both cases a dark-green solution for injection with a concentration of 5 mg/ml (0.5 % w/v). If an incompatibility is noted in the form of unclear solution then the reconstituted solution should be discarded. Visually inspect the reconstituted solution. Only use clear solutions free from visible particles.

This medicinal product is for single use only.

The reconstituted solution is clear and free from visible particles.

Diagnostic procedures with Verdye should be performed under the supervision of a physician. Verdye is intended for intravenous injection via an injection needle, a central or peripheral catheter or cardiac catheter.

The administration and site of Verdye are of critical importance for the quality of the measurements. In principle, for obtaining optimal quality first pass indicator dilution curves, the injection should be as close as possible to the vascular bed, organ or tissue of interest.

On peripheral injection the injection should be made immediately after application of tourniquet and the arm should be raised after release of tourniquet. This ensures rapid transport of the dye from the site of injection and peripheral injection is then practically equivalent to central venous injection.

Dosage

Single dose per measurement in adults, elderly, children:

Cardiac, circulatory, micro-circulatory and tissue perfusion diagnostics as well as **cerebral blood flow**: 0.1 to 0.3 mg/kg body weight as bolus injection

Liver function diagnostics: 0.25 – 0.5 mg/kg body weight as bolus injection

Ophthalmic angiography: 0.1 to 0.3 mg/kg body weight as bolus injection

Total daily dose:

Adults, elderly, adolescents 11-18 years:

The total daily dose of Verdye should be kept below 5 mg/kg body weight.

Children 2 – 11 years:

The total daily dose should be kept below 2.5 mg/kg body weight.

Children 0 - 2 years:

The total daily dose should be kept below 1.25 mg/kg body weight.

Contraindications

Verdye is contraindicated for safety reasons in:

- patients with hypersensitivity to indocyanine green or to sodium iodide unless special precautions are taken,
- patients with hypersensitivity to iodine,
- patients with hyper-thyroidism, patients with autonomic thyroid adenomas
- as in-vitro experiments have shown that indocyanine green displaces bilirubin from its protein binding, Verdye should not be used in premature infants or neonates in whom an exchange transfusion is indicated due to of hyper-bilirubinemia,
- if injection of Verdye was poorly tolerated in the past it must not be used again, since severe anaphylactic reactions might occur.

For full prescribing information go to www.diagnosticgreen.com