

> Benefits of ProveDye® as a marker for intraoperative visualisation ⁽¹⁾

*** SURGICAL INJURIES VISUALISATION**

- > "100% of surgeons are satisfied or very satisfied with PROVEDYE® tissue visualisation." * ⁽³⁾
- > PROVEDYE® may help to prevent post-operative complications resulting from intraoperative injuries. * ⁽³⁾

*** SURGICAL PROCEDURE ACCURACY**

- > "Surgeons consider that complications may be avoided during procedures by using PROVEDYE®." * ⁽³⁾
- > Blue dyes may help to limit the occurrence of post operative complications. ⁽²⁾

Examples of intraoperative surgical visualisations ⁽¹⁾

Leakage visualisation	Intraoperative seal tests
Bladder or ureter visualisation	Delineation of fistula track

* PROVEDYE® staining intensity can be adapted to the needs of the surgeons with the dilution ⁽³⁾

* Retrospective survey study on 37 surgeons and 105 surgical procedures performed in France.

Provepharm
Life Solutions

ProveDye®
Methylene Blue 0,5%



> Product Characteristics ⁽¹⁾

- * Shelf-life: 3 years
- * Pack of 5 ampoules 10 ml
- * For local injection and oral administration

DISTRIBUTOR AND CONTACT:

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CE 2797

References:

- 1) ProveDye® 0,5% - Instruction for use
- 2) Blue Dyes Market study 2017, study executive summary : survey performed on 306 hospital pharmacists, surgeons, OR nurses, gynecologist, urologists and gastroenterologists in Germany, UK and USA*.
- 3) ProveDye® customer survey 2017, study executive summary: survey performed on 37 surgeons in France and 105 surgical procedures in France analysed retrospectively

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ProveDye®
Methylene Blue 0,5%

> To see the invisible...

Marker for surgical visualisation such as intraoperative seal tests, leakages visualisation and delineation of the fistula tract. ⁽¹⁾

Medical device CE Marked - Class IIa.⁽¹⁾



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Ethypharm

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ProveDye®

Methylene Blue 0,5%

> To see the invisible...

* Achieve a convenient colouration with a well established dye

- > Methylene blue is the surgeon's preferred blue dye for surgical marking* (2)
- > 100% of surgeons using PROVEDYE® are satisfied with tissue visualisation, duration and intensity of colouration** (3)

* Choose the pharmaceutical grade methylene blue

- > Provepharm Life Solutions patented an innovative synthesis pathway to produce a vitalized Methylene Blue compound.
- > A unique concentration of 0,5% due to the high level of purity of the methylene blue compound.

* Make a clear choice with PROVEDYE®

- > Methylene blue sterile solution for local and oral use (1)



> Uses of ProveDye® (1)

PROVEDYE®	USE	METHOD OF ADMINISTRATION (route of administration and proposed dilution)	
ALL SURGICAL DEPARTMENTS	Bladder leaks visualisation	Local injection via a urinary catheter (Foley)	200 – 300 ml of a ProveDye® solution diluted in normal saline solution
	Cysts delineation	Local injection directly into the cyst	0.1 to 0.5 ml of ProveDye® solution directly
URO GYNECOLOGICAL AND BREAST SURGERY	Intraoperative delineation of vagino/uretero-vesical or colorecto-vesical fistula tract	Local injection	200 – 300 ml of a ProveDye® solution diluted in normal saline solution at 2 to 0.05%
	Ureter leaks and anastomosis visualisation during colorectal or vascular surgery	Local retrograde injection via a urinary catheter	ProveDye® solution diluted in normal saline solution at around 0.05%
	Visualisation during transaxillar endoscopy in breast surgery	Local injection directly into the infra-mammary fold	1 to 3 ml of ProveDye® solution directly
	Nipple discharge visualisation	Local injection directly into the breast duct	1 to 3 ml of ProveDye® solution directly
GASTRO-DIGESTIVE SURGERY	Colon & bile leakage visualisation	Local injection via a catheter	1 to 20 ml of a ProveDye® solution diluted in normal saline solution at 5 to 0.02% dilution
	Gastric & pancreatic leakage visualisation	Oral administration or via nasogastric tube	ProveDye® solution diluted in water for injection
ENT-ENDOCRINE SURGERY	Intraoperative delineation of anal fistula tract	Local injection directly in the external opening	ProveDye® solution directly
	Parathyroid glands identification	Local administration	1 ml of ProveDye® solution directly
	Temporalis fascia graft visualisation	Local injection directly into the graft	2 ml of ProveDye® solution directly
	Tracheo-oesophageal leakage visualisation	Oral administration or via endotracheal tube or oesophageal catheter	ProveDye® solution diluted in water for injection
	Intraoperative delineation of trachea-oesophageal fistula tract		

ProveDye®

Methylene Blue 0,5%



INSTRUCTIONS FOR USE*

INDICATION:

Marker for surgical visualisation such as intraoperative seal tests, leakages visualisation and delineation of the fistula tract

METHOD OF ADMINISTRATION AND DOSAGE:

The 0,5% Methylene Blue sterile solution can be administered :
 - Directly in local injection,
 - In local injection diluted in normal saline solution,
 - In oral administration diluted in water.

PROVEDYE® must be used immediately after opening or dilution.
 The PROVEDYE® dilution and volume to be administered depends on the destination of the coloration.
 PROVEDYE® could be diluted until 0.01%.

CONTRAINDICATIONS:

Do not administer PROVEDYE® :
 > in case of known hypersensitivity to the methylene blue or to any other thiazine dyes,
 > in case of previous or ongoing treatment with Selective Serotonin Reuptake Inhibitors (SSRIs), bupropion, buspirone, clomipramine, mirtazapine and venlafaxine,
 > in case of Glucose-6-Phosphate Dehydrogenase deficiency,
 > in case of pregnancy or breastfeeding PROVEDYE® should be avoided
 In case of moderate or severe renal disease, patients must be closely monitored.

WARNINGS AND PRECAUTIONS:

> PROVEDYE® must be used by a healthcare professional.
 > A preoperative assessment is recommended before using PROVEDYE®
 > Protective measures against patient exposure to strong light, including that within instruments such as pulse oximeters should be taken, because there is a risk of cutaneous photosensitivity reaction.
 > The wearing of gloves is recommended for users.
 > Do not use a damaged ampoule of PROVEDYE®. Do not use PROVEDYE® if the solution is colourless.
 > PROVEDYE® must be used immediately after opening or dilution.

> Do not inject PROVEDYE® intravenously, subcutaneously, intrathecally, intra-amniotically or intraocularly.
 > PROVEDYE® is for single use only: discard any remaining solution after opening.
 > In case of re-use of PROVEDYE®, there is a risk to loss sterility due to potential contamination of the sterile solution (it is considered as a decrease of technical performance).
 > PROVEDYE® should be disposed of in clinical waste.

ADVERSE EFFECTS:

> Gastrointestinal: nausea, vomiting, diarrhea, abdominal pain, blue colour of faeces and saliva.
 > Hematologic: hemolysis (in glucose-6-phosphate dehydrogenase deficiency, or high doses), methemoglobinemia (after high doses), hyperbilirubinemia.
 > Cardiovascular: hypertension, hypotension, arrhythmia, chest pain.
 > Body as a whole: profuse sweating.
 > Dermal: rash (blue macules, severe burning pain), skin discoloration, urticaria, increased sensitivity of the skin to the light (photosensitivity).
 > Nervous system: headaches, dizziness, mental confusion, anxiety, tremor, fever, aphasia, agitation; serotonin syndrome when certain medicines to treat depression or anxiety have been taken
 > Administration site: thrombophlebitis, (resulting from high doses, if not adequately diluted – not more than 350 mg of methylene blue should be diluted in each 500 mL of infusion fluid), necrosis (if extravasation occurs).
 > Renal: blue colour of urine.
 > Respiratory, thoracic and mediastinal: dyspnea, tachypnea, hypoxia.
 > Ophthalmic: mydriasis.
 > Immune: anaphylactic reaction.
 > Oral administration may cause gastrointestinal disturbances and dysuria.
 > Use of methylene blue for endoscopic tattoo has been associated with vascular necrosis, mucosal ulceration, mural necrosis, extramural fat necrosis and inflammatory changes in the colon.

* Methylene Blue is preferred to other blue dyes for intraoperative delineation of fistula tract: in 90% of cases for vesicovaginal and rectovaginal fistulae (N=40) and in 84% of cases for anal fistulae (N=69). Survey performed on 306 hospital pharmacists, surgeons, OR nurses, gynaecologists, urologists and gastroenterologists in Germany, UK and USA

** 100% of the 37 interviewed users were very satisfied (24%) or satisfied (76%) with PROVEDYE® tissue Visualisation and 100% of surgeons using ProveDye® are satisfied with duration and intensity of colouration. Retrospective survey study performed on 37 surgeons and 105 procedures in France.