

**COMPOSITION:**

Each ampoule of PROVEDYE® 0.5% sterile solution contains 50 mg of Methylene Blue (Proveblue®) diluted in 10 mL of water for injections.

**INDICATIONS:**

**Marker for surgical visualisation such as intra operative seal tests, leakage visualisation, delineation of fistula tract and visualisation of Sentinel Lymph Nodes (SLN) in oncologic surgery.**

**CONTRAINDICATIONS:**

Do not administer PROVEDYE®:

- In case of known hypersensitivity to methylene blue or to any other thiazine dyes,
- In case of recent (end of treatment less than a month ago) or ongoing treatment with Selective Serotonin Reuptake Inhibitors (SSRIs), Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs), Monoamine Oxidase Inhibitors (MAOI), bupropion, buspirone, clomipramine, mirtazapine and venlafaxine,
- In case of Glucose-6-Phosphate Dehydrogenase deficiency,

In case of pregnancy or breastfeeding, PROVEDYE® should be avoided.

**ADMINISTRATION ROUTE:**

PROVEDYE® is administered locally.

**METHOD OF ADMINISTRATION AND DOSAGE:**

PROVEDYE® can be administered through local injection, undiluted or diluted in isotonic saline solution.

For visualisation of Sentinel Lymph Nodes (SLN) in oncologic surgery, PROVEDYE® must be diluted in isotonic saline solution, prior being administered through local injection.

PROVEDYE® must be used immediately after opening or dilution.

PROVEDYE® dilution and volume to be administered depend on the destination of the colouration.

PROVEDYE® could be diluted until 0.01%. For example: for a 0.01% dilution, dilute 2 parts of PROVEDYE® 0.5% with 100 parts of isotonic saline solution; for a 1.25 mg/mL dilution in isotonic saline solution, dilute 1 part of PROVEDYE® 0.5% with 3 parts of isotonic saline solution.

*Details on recommendations on method of administration according to the use are presented in section SPECIAL PRECAUTIONS FOR USE.*



**ProveDye®**

Methylene blue 0.5%

**SPECIAL PRECAUTIONS FOR USE**

(Document to keep in the operative theatre)

**PROVEDYE® 0.5% sterile solution**

Preparation for local administration. Do not inject PROVEDYE® intravenously, intrathecally, intra-amniotically or intraocularly.

PROVEDYE® may be diluted in isotonic saline solution for local injection.

PROVEDYE® must be used immediately after opening or dilution.

PROVEDYE® can be diluted until 0.01%. For example: for a 0.01% dilution, dilute 2 parts of PROVEDYE® 0.5% with 100 parts of isotonic saline solution; for a 1.25 mg/mL dilution in isotonic saline solution, dilute 1 part of PROVEDYE® 0.5% with 3 parts of isotonic saline solution.

Any unused product or waste material should be disposed of in accordance with local requirements.

**TABLE OF USAGE EXAMPLES:**

PROVEDYE®	USE	METHOD OF ADMINISTRATION (Proposed route of administration and dilution)	
BREAST SURGERY	Visualisation of sentinel lymph nodes in breast cancer	Peritumoral or subareolar injection	2 mL (or less) of 1.25 mg/mL solution of PROVEDYE® diluted in isotonic saline solution
	Visualisation during transaxillar endoscopy in breast surgery	Local injection directly into the infra-mammary fold	1 mL of undiluted PROVEDYE® solution
	Nipple discharge visualisation	Local injection directly into the breast duct	2 mL of undiluted PROVEDYE® solution
URO-GYNECOLOGICAL SURGERY	Visualisation of sentinel lymph nodes in endometrial or cervical cancer	Uterine Cervix injection	1 mL of 2.5 mg/mL solution of PROVEDYE® diluted in isotonic saline solution
	Intra-operative delineation of vagino/utero-vesical or colorecto-vesical fistula tract	Local injection	200 – 300 mL of diluted PROVEDYE® solution in isotonic saline solution
	Ureter leaks and anastomosis visualisation during colorectal or vascular surgery	Local retrograde injection via a urinary catheter	Diluted PROVEDYE® solution in isotonic saline solution
OTHER SURGERY	Pilonidal sinus visualisation	Local injection into the pilonidal sinus	2 to 4 mL of solution of PROVEDYE® undiluted or diluted in isotonic saline solution
	Bladder leaks visualisation	Local injection via a urinary catheter (Foley)	200 – 300 mL of diluted PROVEDYE® solution in isotonic saline solution
	Cysts delineation	Local injection directly into the cyst	0.1 to 0.5 mL of undiluted PROVEDYE® solution
	Visualisation of sentinel lymph nodes in melanoma	Peritumoral, intradermal injection	Less than 1 mL of 1.25 mg/mL or 2.5 mg/mL solution of PROVEDYE® in isotonic saline solution

## WARNINGS AND PRECAUTIONS:

- PROVEDYE® must be administered by a Healthcare Professional.
- In case of moderate or severe renal disease patients must be closely monitored.
- 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 PROVEDYE® 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, 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 lose 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: haemolysis (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 discolouration, urticaria, increased sensitivity of the skin to the light (photosensitivity).
- Central 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, necrosis (resulting from high doses, if not adequately diluted).
- Renal: blue colour of urine.
- Respiratory, thoracic and mediastinal: dyspnea, tachypnea, hypoxia.
- Ophthalmic: mydriasis.
- Immune: anaphylactic reaction.

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.

### Note to the user

Any serious incident that has occurred in relation to the device should be reported to the manufacturer at [safety@provepharm.com](mailto:safety@provepharm.com) and the competent authority of the Member State in which the user is established.

### SHELF-LIFE:

48 months.

### CONDITIONING:

10 mL ampoules, in packs of 5 ampoules.

### STORAGE:

Do not refrigerate PROVEDYE® under 8°C.  
Do not freeze. Keep the ampoule in the original package to protect it from light.

### PUBLICATION DATE:

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## ProveDye®

Methylene blue 0.5%

## SPECIAL PRECAUTIONS FOR USE

(Document to keep in the operative theatre)

### PROVEDYE® 0.5% sterile solution

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### TABLE OF USAGE EXAMPLES:

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GASTRO-DIGESTIVE SURGERY	Colon & bile leakage visualisation	Local injection via a catheter	1 to 20 mL of a diluted PROVEDYE® solution in isotonic saline solution
	Intra-operative delineation of anal fistula tract	Local injection directly in the external opening	Undiluted PROVEDYE® solution
ENDOCRINE SURGERY	Visualisation of sentinel lymph nodes in thyroid cancer	Peritumoral injection	Up to 0.5 mL diluted PROVEDYE® solution in isotonic saline solution
	Parathyroid glands identification	Local administration	1 mL of undiluted PROVEDYE® solution