

Instruction for use



COMPOSITION:

Each ampoule of PROVEDYE® 0.5% contains 10 mg of **Methylene Blue (Proveblue®)** diluted in 2 ml of water solution for injection.

INDICATIONS:

Marker for surgical visualization such as intra operative seal tests, leakages visualization 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%.

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

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.



SPECIAL PRECAUTIONS FOR USE



(to keep in the operative theatre)

Methylene Blue 0,5%

PROVEDYE® 0.5% 2 ml - Sterile solution.

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

PROVEDYE® may be diluted in water (for oral use only) or in normal saline solution and must be used immediately after opening or dilution. PROVEDYE® could be diluted until 0.01%. Any unused product or waste material should be disposed of in accordance with local requirements.

PROVEDYE®	USE	METHOD OF ADMINISTRATION (route of administration and proposed dilution)	
ALL SURGICAL DEPARTMENTS	Bladder leaks visualization	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	Intra-operative 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 visualization during colorectal or vascular surgery	Local retrograde injection via a urinary catheter	ProveDye® solution diluted in normal saline solution at around 0.05%
	Visualization during transaxillar endoscopy in breast surgery	Local injection directly into the infra-mammary fold	1 to 3 ml of ProveDye® solution directly
	Nipple discharge visualization	Local injection directly into the breast duct	1 to 3 ml of ProveDye® solution directly



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.

STORAGE:

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

CONDITIONING:

2 ml ampoules, in packs of 5 or 20 ampoules.

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Provepharm*
Life Solutions

ProveDye®

Methylene Blue 0,5%

SPECIAL PRECAUTIONS FOR USE

(to keep in the operative theatre)

PROVEDYE® 0.5% 2 ml - Sterile solution.

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

PROVEDYE® may be diluted in water (for oral use only) or in normal saline solution and must be used immediately after opening or dilution. PROVEDYE® could be diluted until 0.01%.

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

PROVEDYE®	USE	METHOD OF ADMINISTRATION (route of administration and proposed dilution)	
GASTRO-DIGESTIVE SURGERY	Colon & bile leakage visualization	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 visualization	Oral administration or via nasogastric tube	ProveDye® solution diluted in water for injection
	Intra-operative delineation of anal fistula tract	Local injection directly in the external opening	ProveDye® solution directly
ENT-ENDOCRINE SURGERY	Parathyroid glands identification	Local administration	1 ml of ProveDye® solution directly
	Temporalis fascia graft visualization	Local injection directly into the graft	2 ml of ProveDye® solution directly
	Tracheo-oesophageal leakage visualization	Oral administration or via endotracheal tube or oesophageal catheter	ProveDye® solution diluted in water for injection
	Intra-operative delineation of trachea-oesophageal fistula tract		

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