# Instruction for use

ProveDye® 0,5%
Methylene blue

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

**INDICATIONS:**
**Visualization aid for surgical procedures such as:**
- **Delineation of tissues and operative pieces,**
- **Seal test for sutures, detection of leaks,**
- **Fistula detection.**

**METHOD OF ADMINISTRATION AND DOSAGE:**
A preoperative assessment is recommended before using PROVEDYE®.
PROVEDYE® may be diluted in water (for oral use only) and in sodium chloride (NaCl) 0.9% solution and must be used immediately after dilution.
The PROVEDYE® dilution and volume to be administrated depends on the destination and size of the area to be coloured. PROVEDYE® could be diluted until 0.01%.
PROVEDYE® may be placed in contact with the anatomic structure after dilution.
PROVEDYE® can also be injected in the light of certain organs, or placed in contact with the epithelium of the organ via the existing natural orifices.
PROVEDYE® can also be administered orally after dilution.

**CONTRAINDICATIONS:**
Do not administrate PROVEDYE®:
- in case of known hypersensitivity to the methylene blue or to any other thiazine dyes,
- in case of immediately, previous or ongoing treatment with Selective serotonin reuptake inhibitors (SSRIs), bupropion, buspirone, clomipramine, mirtazapine and venlafaxine,
- in case of Pregnancy or breastfeeding PROVEDYE® should be avoided,
- in case of Glucose-6-Phosphate Dehydrogenase deficiency.

In case of moderate or severe renal disease patients must be closely monitored.

Provepharm Life Solutions CE 0086 STERILE STERILIZE 8° C

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**SPECIAL PRECAUTIONS FOR USE**

(to keep in the operative theatre)

**PROVEDYE® 0.5% 2ml - Sterile solution.**
Preparation for local or oral administration.
Do not inject PROVEDYE® in intravenous, subcutaneous, intrathecal, intra-amniotic or intraocular injection.
PROVEDYE® may be diluted in water (for oral use only) or in sodium chloride (NaCl) 0.9% solution and must be used immediately after dilution. PROVEDYE® could be diluted until 0.01%.
Additional information on the way in which PROVEDYE® can be administered is provided in the Instructions for use.
Use immediately after opening. Any unused product or waste material should be disposed of in accordance with local requirements.

| | USE OF PROVEDYE® | METHOD OF ADMINISTRATION | FISTULA | LEAKAGE | DELINEATION |
|---|---|---|---|---|---|
| URO-GYNECO SURGERY | • Ureterovesical fistula detection<br>• Vesicovaginal fistula detection<br>• Colo-vesical fistula detection<br>• Rectourethral fistula detection | ➢ Via an urinary catheter<br>➢ Into the vagina during a cystoscopy (200 mL of diluted ProveDye®)<br>➢ Via an urinary catheter<br>➢ Via an urethral catheter | X | | |
| | • Ureter leakage detection<br>• Vesicourethral anastomosis detection | ➢ Via a urinary catheter (5 mL of diluted ProveDye® in normal saline solution) | | X | |
| | • Identification of the processus patent vaginalis (PPV) and prevention of hydrocele<br>• Localization aid of tunical and urethral tears in corpora cavernosa | ➢ In hydrocele (between tunica vaginalis and albugina) (0.6-6 mL of ProveDye®)<br>➢ Into the corpora cavernosa via the urethral meatus | | | X |
| GASTRO-DIGESTIVE SURGERY | • Anal fistula detection<br>• Colo-vesical fistula detection<br>• Rectourethral fistula detection<br>• Oesophagial fistula detection | ➢ Via an external catheter<br>➢ Via an urinary catheter<br>➢ Via an urethral catheter<br>➢ Via oral administration (4 mL of ProveDye® in 30 mL of water) | X | | |
| | • Colon leakage detection<br>• Gastric leakage detection<br>• Bile leakage detection<br>• Pancreatic leakage detection<br>• Esophagus and lung leakage detection | ➢ Via a rectal catheter (1000 mL of normal saline solution containing 20 mL of ProveDye®)<br>➢ Via a nasogastric tube<br>➢ Via a catheter (4 mL of ProveDye® in 20 mL of normal saline solution)<br>➢ Local administration and via oesophageal catheter (4-40 mL of ProveDye® diluted in 20-1000 mL of water or normal saline solution) | | X | |

**WARNINGS:**
Do not inject PROVEDYE® intravenously, subcutaneously, intrathecally, intra-amniotically or intraocularly. Do not use PROVEDYE® if the solution is colourless.
Do not use a damaged ampoule of Provedye®.
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.

**PRECAUTIONS:**
PROVEDYE® must be used by a healthcare professional.

The wearing of gloves is recommended for users.
PROVEDYE® must be used immediately after opening or dilution.
Protective measures against exposure to strong light, including that within instruments such as pulse oxymeters should be taken, because there is a risk of cutaneous photosensitivity reaction.

**ADVERSE EFFECTS:**

- Gastrointestinal: nausea, vomiting, diarrhea, abdominal pain, blue colour of faeces and saliva.
- Hematologic: hemolysis (in glucose-6-phosphate dehydrogenase defi ciency, 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.
- Ophtalmic: 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 or freeze.
Keep the ampoule in the original package to protect it from light.

**CONDITIONING:**
2 ml ampoules, in packs of 5 or 20 ampoules.

**PUBLICATION DATE :**
Last revision : 11-2018.

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Provepharm Life Solutions

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## SPECIAL PRECAUTIONS FOR USE

(to keep in the operative theatre)

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| | USE OF PROVEDYE® | METHOD OF ADMINISTRATION | FIS-TULA | LEAK-AGE | DELIN-EATION |
|---|---|---|---|---|---|
| GENERAL SURGERY | • Delineation of cysts | ➢ Directly into the cyst (0,2 mL of ProveDye®) | | | X |
| BREAST SURGERY | • Visualisation aid during transaxillar en-doscopy<br>• Visualization aid for nipple discharge | ➢ At the infra-mammary fold (1-2 mL of ProveDye®)<br>➢ Directly into the breast duct (2-6 mL of ProveDye®) | | | X |
| ENDOCRINE SURGERY | • Identification of the parathyroid glands, re-current nerves and inferior thyroid arteries | ➢ Local administration (1 mL of ProveDye®) | | | X |
| ENT SURGERY | • Preauricular sinuses (PAS) and branchial sinuses fistula (BSF) detection<br>• Tracheoesophageal/Esophagorespiratory fistulae detection | ➢ (2-6 mL of ProveDye®)<br>➢ Via an endotracheal tube during a bronchoscopy | X | | |
| | • Stain of temporalis fascia graft | ➢ Directly into the graft (2 mL of ProveDye®) | | | X |