# Instruction for use

ProveDye®
Methylene Blue 0,5%

**COMPOSITION:**
Each ampoule of PROVEDYE® 0.5% contains 50 mg of **Methylene Blue (Proveblue®)** diluted in 10 ml of water for injection.

**INDICATIONS:**
**Marker for surgical visualisation such as intra operative 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 depend on the destination of the coloration. PROVEDYE® could be diluted until 0.01%. For this, dilute 2 parts of PROVEDYE® 0.5% with 100 parts of normal saline solution or water.
*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.

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**SPECIAL PRECAUTIONS FOR USE**

(to keep in the operative theatre)

**PROVEDYE® 0.5% 10 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%. For this, dilute 2 parts of PROVEDYE® 0.5% with 100 parts of normal saline solution or water. Any unused product or waste material should be disposed of in accordance with local requirements.

| **PROVEDYE®** | **USE** | **METHOD OF ADMINISTRATION** | |
|---|---|---|---|
| **ALL SURGICAL DEPARTMENTS** | **Bladder leaks visualisation** | Local injection via a urinary catheter (Foley) | 200 – 300 ml of diluted ProveDye® solution |
| | **Cysts delineation** | Local injection directly into the cyst | 0.1 to 0.5 ml of undiluted ProveDye® solution |
| **URO-GYNECOLOGICAL AND BREAST SURGERY** | **Intra-operative delineation of vagino/utero-vesical or colorecto-vesical fistula tract** | Local injection | 200 – 300 ml of diluted ProveDye® solution |
| | **Ureter leaks and anastomosis visualisation** during colorectal or vascular surgery | Local retrograde injection via a urinary catheter | Diluted ProveDye® solution |
| | **Visualization 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 |

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**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.
> 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. Do not freeze.
Keep the ampoule in the original package to protect it from light.

**CONDITIONING:**
10 ml ampoules, in packs of 5 ampoules.

**PUBLICATION DATE :**
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**Provepharm S.A.S.**
**22 Rue Marc Donadille 13013 Marseille, France**
www.provepharm.com

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| PROVEDYE® | USE | METHOD OF ADMINISTRATION | |
|---|---|---|---|
| **GASTRO-DIGESTIVE SURGERY** | **Colon & bile leakage visualisation** | Local injection via a catheter | 1 to 20 ml of diluted ProveDye® solution |
| | **Gastric & pancreatic leakage visualisation** | Oral administration or via nasogastric tube | Diluted ProveDye® solution |
| | **Intra-operative delineation of anal fistula tract** | Local injection directly in the external opening | Undiluted ProveDye® solution |
| **ENT-ENDOCRINE SURGERY** | **Parathyroid glands identification** | Local administration | 1 ml of undiluted ProveDye® solution |
| | **Temporalis fascia graft visualisation** | Local injection directly into the graft | 2 ml of undiluted ProveDye® solution |
| | **Tracheo-oesophageal leakage visualisation** | Oral administration or via endotracheal tube or oesophageal catheter | Diluted ProveDye® solution |
| | **Intra-operative delineation of trachea-oesophageal fistula tract** | | |

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