

# Instruction for use



**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 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.



**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  | FIS-TULA | LEAK-AGE | DELIN-EATION |
|--------------------------|--|---|----------|----------|--------------|
| URO-GYNECO SURGERY       | <ul style="list-style-type: none"> <li>• Ureterovesical fistula detection</li> <li>• Vesicovaginal fistula detection</li> </ul>  | <ul style="list-style-type: none"> <li>&gt; Via an urinary catheter</li> <li>&gt; Into the vagina during a cystoscopy (200mL of diluted Methylene Blue)</li> <li>&gt; Via an urinary catheter</li> <li>&gt; Via an urethral catheter</li> </ul>   | <b>X</b> |          |              |
|                          | <ul style="list-style-type: none"> <li>• Colo-vesical fistula detection</li> <li>• Rectourethral fistula detection</li> </ul>  | <ul style="list-style-type: none"> <li>&gt; Via a urinary catheter (5mL of diluted Methylene Blue in normal saline solution)</li> </ul>   |          | <b>X</b> |              |
|                          | <ul style="list-style-type: none"> <li>• Identification of the processus patent vaginalis (PPV) and prevention of hydrocele</li> <li>• Localization aid of tunical and urethral tears in corpora cavernosa</li> </ul>                      | <ul style="list-style-type: none"> <li>&gt; In hydrocele (between tunica vaginalis and albugina) (0.6-6mL of Methylene Blue)</li> <li>&gt; Into the corpora cavernosa via the urethral meatus</li> </ul>  |          |          | <b>X</b>     |
| GASTRO-DIGESTIVE SURGERY | <ul style="list-style-type: none"> <li>• Anal fistula detection</li> <li>• Colo-vesical fistula detection</li> <li>• Rectourethral fistula detection</li> <li>• Oesophageal fistula detection</li> </ul>                                   | <ul style="list-style-type: none"> <li>&gt; Via an external catheter</li> <li>&gt; Via an urinary catheter</li> <li>&gt; Via an urethral catheter</li> <li>&gt; Via oral administration (4mL of Methylene Blue in 30mL of water)</li> </ul>   | <b>X</b> |          |              |
|                          | <ul style="list-style-type: none"> <li>• Colon leakage detection</li> <li>• Gastric leakage detection</li> <li>• Bile leakage detection</li> <li>• Pancreatic leakage detection</li> <li>• Esophagus and lung leakage detection</li> </ul> | <ul style="list-style-type: none"> <li>&gt; Via a rectal catheter (1000mL of normal saline solution containing 20mL of Methylene Blue)</li> <li>&gt; Via a nasogastric tube</li> <li>&gt; Via a catheter (4mL of Methylene Blue in 20 mL of normal saline solution)</li> <li>&gt; Local administration and via oesophageal catheter (4-40mL of Methylene Blue diluted in 20-1000mL of water or normal saline solution)</li> </ul> |          | <b>X</b> |              |

**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.

**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, urticarial.
- Nervous system : headaches, dizziness, mental confusion, anxiety, tremor, fever, aphasia, agitation.
- 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.
- Ophthalmologic: 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 :**

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

**PUBLICATION DATE :**

Last revision : 11-2017.



**Provepharm S.A.S. 22 Rue Marc Donadille 13013 Marseille, France**

[www.provepharm.com](http://www.provepharm.com)

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|--------------------------|--|--|----------|----------|--------------|
| <b>GENERAL SURGERY</b>   | • Delineation of cysts   | ➢ Directly into the cyst (0.2mL of Methylene Blue)   |          |          | <b>X</b>     |
| <b>BREAST SURGERY</b>    | • Visualisation aid during transaxillar endoscopy<br>• Visualization aid for nipple discharge  | ➢ At the infra-mammary fold (1-2mL of Methylene Blue)<br>➢ Directly into the breast duct (2-6mL of Methylene Blue) |          |          | <b>X</b>     |
| <b>ENDOCRINE SURGERY</b> | • Identification of the parathyroid glands, recurrent nerves and inferior thyroid arteries   | ➢ Local administration (1mL of Methylene Blue)   |          |          | <b>X</b>     |
| <b>ENT SURGERY</b>       | • Preauricular sinuses (PAS) and branchial sinuses fistula (BSF) detection<br>• Tracheoesophageal/Esophagorespiratory fistulae detection | ➢ (2-6mL of Methylene Blue)<br>➢ Via an endotracheal tube during a bronchoscopy                                    | <b>X</b> |          |              |
|                          | • Stain of temporalis fascia graft   | ➢ Directly into the graft (2mL of Methylene Blue)  |          |          | <b>X</b>     |