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 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.

CE 2797 STERILE STERILIZE 8° C Provepharm Life Solutions

SPECIAL PRECAUTIONS FOR USE

ProveDye®
Methylene Blue 0,5%

(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%. 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

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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 :
Last revision : 03-2019.

Provepharm S.A.S.
22 Rue Marc Donadille 13013 Marseille, France
www.provepharm.com

Provepharm
Life Solutions

ProveDye®
Methylene Blue 0,5%

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%.
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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Instruction for use

ProveDye® 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 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

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 • Vesicovaginal fistula detection • Colo-vesical fistula detection • Rectouretrhal fistula detection	➢ Via an urinary catheter ➢ Into the vagina during a cystoscopy (200mL of diluted Methylene Blue) ➢ Via an urinary catheter ➢ Via an urethral catheter	X		
	• Ureter leakage detection • Vesicourethral anastomosis detection	➢ Via a urinary catheter (5mL of diluted Methylene Blue in normal saline solution)		X	
	• Identification of the processus patent vaginalis (PPV) and prevention of hydrocele • Localization aid of tunical and urethral tears in corpora cavernosa	➢ In hydrocele (between tunica vaginalis and albugina) (0.6-6mL of Methylene Blue) ➢ Into the corpora cavernosa via the urethral meatus			X
GASTRO-DIGESTIVE SURGERY	• Anal fistula detection • Colo-vesical fistula detection • Rectouretrhal fistula detection • Oesophagial fistula detection	➢ Via an external catheter ➢ Via an urinary catheter ➢ Via an urethral catheter ➢ Via oral administration (4mL of Methylene Blue in 30mL of water)	X		
	• Colon leakage detection • Gastric leakage detection • Bile leakage detection • Pancreatic leakage detection • Esophagus and lung leakage detection	➢ Via a rectal catheter (1000mL of normal saline solution containing 20mL of Methylene Blue) ➢ Via a nasogastric tube ➢ Via a catheter (4mL of Methylene Blue in 20 mL of normal saline solution) ➢ Local administration and via oesophageal catheter (4-40mL of Methylene Blue diluted in 20-1000mL 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.

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.
- Ophtalmologic: 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

Provepharm Life Solutions

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

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