Previous Versions Product Information

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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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%. 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 :
IFU version 2 - Last revision : 10/2020

Provepharm S.A.S.
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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%. 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	
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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Instruction for use

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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,
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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%. 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:
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> 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.
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> 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).
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> Immune: anaphylactic reaction.
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> 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.

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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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