Previous Versions Product Information

EN – Instructions for use

ProveDye®
Methylene Blue 0,5%

COMPOSITION:
Each ampoule of PROVEDYE® 0.5% sterile solution 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, leakage visualisation, delineation of fistula tract and visualisation of Sentinel Lymph Nodes (SLN) in oncologic surgery.

CONTRAINDICATIONS:
Do not administer PROVEDYE®:
- In case of known hypersensitivity to methylene blue or to any other thiazine dyes,
- In case of recent (end of treatment less than one month ago) or ongoing treatment with Selective Serotonin Reuptake Inhibitors (SSRIs), Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs), Monoamine Oxidase Inhibitors (MAOI), bupropion, buspirone, clomipramine, mirtazapine and venlafaxine,
- In case of Glucose-6-Phosphate Dehydrogenase deficiency,

In case of pregnancy or breastfeeding, PROVEDYE® should be avoided.

METHOD OF ADMINISTRATION AND DOSAGE:
PROVEDYE® can be administered:
- Through local injection, undiluted or diluted in isotonic saline solution,
- Through oral administration, diluted in water.

For visualisation of Sentinel Lymph Nodes (SLN) in oncologic surgery, PROVEDYE® must be diluted in isotonic saline solution, prior being administered through local injection.

PROVEDYE® must be used immediately after opening or dilution.
PROVEDYE® dilution and volume to be administered depend on the destination of the coloration.
PROVEDYE® could be diluted until 0.01%. For example: for a 0.01% dilution, dilute 2 parts of PROVEDYE® 0.5% with 100 parts of isotonic saline solution or water; for a 1.25 mg/mL dilution in isotonic saline solution, dilute 1 part of PROVEDYE® 0.5% with 3 parts of isotonic saline solution.

Details on recommendations on method of administration according to the use are presented in section SPECIAL PRECAUTIONS FOR USE.

CE 2797 | STERILE | 2 STERILIZE | 8° C

ProveDye®
Methylene Blue 0,5%

SPECIAL PRECAUTIONS FOR USE

(Document to keep in the operative theatre)

PROVEDYE® 0.5% sterile solution
Preparation for local or oral administration. Do not inject PROVEDYE® intravenously, intrathecally, intra-amniotically or intraocularly.
PROVEDYE® may be diluted in water (for oral use only), or in isotonic saline solution.
PROVEDYE® must be used immediately after opening or dilution.
PROVEDYE® can be diluted until 0.01%. For example: for a 0.01% dilution, dilute 2 parts of PROVEDYE® 0.5% with 100 parts of isotonic saline solution or water; for a 1.25 mg/mL dilution in isotonic saline solution, dilute 1 part of PROVEDYE® 0.5% with 3 parts of isotonic saline solution.
Any unused product or waste material should be disposed of in accordance with local requirements.

PROVEDYE®	USE	METHOD OF ADMINISTRATION (Proposed route of administration and dilution)	
BREAST SURGERY	**Visualisation of sentinel lymph nodes in breast cancer**	Peritumoral or subareolar injection	2 mL (or less) of 1.25 mg/mL solution of PROVEDYE® diluted in isotonic saline solution
	Visualisation 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
URO-GYNECOLO-GICAL SURGERY	**Visualisation of sentinel lymph nodes in endometrial or cervical cancer**	Uterine Cervix injection	1 mL of 2.5 mg/mL solution of PROVEDYE® diluted in isotonic saline solution
	Intra-operative delineation of vagino/utero-vesical or colorecto-vesical fistula tract	Local injection	200 – 300 mL of diluted PROVEDYE® solution in isotonic saline solution
	Ureter leaks and anastomosis visualisation during colorectal or vascular surgery	Local retrograde injection via a urinary catheter	Diluted PROVEDYE® solution in isotonic saline solution
OTHER SURGERY	**Pilonidal sinus visualisation**	Local injection into the pilonidal sinus	2 to 4 mL of solution of PROVEDYE® undiluted or diluted in isotonic saline solution
	Cysts delineation	Local injection directly into the cyst	0.1 to 0.5 mL of undiluted PROVEDYE® solution
	Bladder leaks visualisation	Local injection via a urinary catheter (Foley)	200 – 300 mL of diluted PROVEDYE® solution in isotonic saline solution
	Visualisation of sentinel lymph nodes in melanoma	Peritumoral, intradermal injection	Less than 1 mL of 1.25 mg/mL or 2.5 mg/mL solution of PROVEDYE® in isotonic saline solution

WARNINGS AND PRECAUTIONS:

- PROVEDYE® must be administered 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 PROVEDYE® 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, 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.
- In case of moderate or severe renal disease patients must be closely monitored.

ADVERSE EFFECTS:

- Gastrointestinal: nausea, vomiting, diarrhea, abdominal pain, blue colour of faeces and saliva.
- Hematologic: haemolysis (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).
- Central 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, necrosis (resulting from high doses, if not adequately diluted).
- 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.

Note to the user

Any serious incident that has occurred in relation to the device should be reported to the manufacturer at safety@provepharm.com and the competent authority of the Member State in which the user is established.

SHELF-LIFE

48 months

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 5 - Last revision: 06/2023.

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

ProveDye®

Methylene Blue 0,5%

SPECIAL PRECAUTIONS FOR USE

(Document to keep in the operative theatre)

PROVEDYE® 0.5% sterile solution

Preparation for local or oral administration. Do not inject PROVEDYE® intravenously, intrathecally, intra-amniotically or intraocularly.
PROVEDYE® may be diluted in water (for oral use only), or in isotonic saline solution.
PROVEDYE® must be used immediately after opening or dilution.
PROVEDYE® can be diluted until 0.01%. For example: for a 0.01% dilution, dilute 2 parts of PROVEDYE® 0.5% with 100 parts of isotonic saline solution or water; for a 1.25 mg/mL dilution in isotonic saline solution, dilute 1 part of PROVEDYE® 0.5% with 3 parts of isotonic saline solution.
Any unused product or waste material should be disposed of in accordance with local requirements.

PROVEDYE®	USE	METHOD OF ADMINISTRATION (Proposed route of administration and dilution)	
GASTRO-DIGESTIVE SURGERY	**Colon & bile leakage visualisation**	Local injection via a catheter	1 to 20 mL of a diluted PROVEDYE® solution in isotonic saline solution
	Gastric & pancreatic leakage visualisation	Oral administration or via nasogastric tube	Diluted PROVEDYE® solution in water for injection
	Intra-operative delineation of anal fistula tract	Local injection directly in the external opening	Undiluted PROVEDYE® solution
ENT-ENDOCRINE SURGERY	**Visualisation of sentinel lymph nodes in thyroid cancer**	Peritumoral injection	Up to 0.5 mL diluted PROVEDYE® solution in isotonic saline solution
	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 via endotracheal tube or oesophageal catheter	Diluted PROVEDYE® solution in water for injection
	Intra-operative delineation of tracheo-oesophageal fistula tract		

EN – Instructions for use

ProveDye®
Methylene Blue 0,5%

COMPOSITION:
Each ampoule of PROVEDYE® 0.5% sterile solution 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, leakage visualisation, delineation of fistula tract and visualisation of Sentinel Lymph Nodes (SLN) in oncologic surgery.

CONTRAINDICATIONS:
Do not administer PROVEDYE®:
- In case of known hypersensitivity to 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.

METHOD OF ADMINISTRATION AND DOSAGE:
PROVEDYE® can be administered:
- Through local injection, undiluted or diluted in isotonic saline solution,
- Through oral administration, diluted in water.

For visualisation of Sentinel Lymph Nodes (SLN) in oncologic surgery, PROVEDYE® must be diluted in isotonic saline solution, prior being administered through local injection.

PROVEDYE® must be used immediately after opening or dilution.
PROVEDYE® dilution and volume to be administered depend on the destination of the coloration.
PROVEDYE® could be diluted until 0.01%. For example: for a 0.01% dilution, dilute 2 parts of PROVEDYE® 0.5% with 100 parts of isotonic saline solution or water; for a 1.25 mg/mL dilution in isotonic saline solution, dilute 1 part of PROVEDYE® 0.5% with 3 parts of isotonic saline solution.

Details on recommendations on method of administration according to the use are presented in section SPECIAL PRECAUTIONS FOR USE.

CE 2797 | STERILE | 2 STERILIZE | 8° C

ProveDye®
Methylene Blue 0,5%

SPECIAL PRECAUTIONS FOR USE

(Document to keep in the operative theatre)

PROVEDYE® 0.5% sterile solution
Preparation for local or oral administration. Do not inject PROVEDYE® intravenously, intrathecally, intra-amniotically or intraocularly.
PROVEDYE® may be diluted in water (for oral use only), or in isotonic saline solution.
PROVEDYE® must be used immediately after opening or dilution.
PROVEDYE® can be diluted until 0.01%. For example: for a 0.01% dilution, dilute 2 parts of PROVEDYE® 0.5% with 100 parts of isotonic saline solution or water; for a 1.25 mg/mL dilution in isotonic saline solution, dilute 1 part of PROVEDYE® 0.5% with 3 parts of isotonic saline solution.
Any unused product or waste material should be disposed of in accordance with local requirements.

PROVEDYE®	USE	METHOD OF ADMINISTRATION (Proposed route of administration and dilution)	
BREAST SURGERY	**Visualisation of sentinel lymph nodes in breast cancer**	Peritumoral or subareolar injection	2 mL (or less) of 1.25 mg/mL solution of PROVEDYE® diluted in isotonic saline solution
	Visualisation 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
URO-GYNECOLO-GICAL SURGERY	**Visualisation of sentinel lymph nodes in endometrial or cervical cancer**	Uterine Cervix injection	1 mL of 2.5 mg/mL solution of PROVEDYE® diluted in isotonic saline solution
	Intra-operative delineation of vagino/utero-vesical or colorecto-vesical fistula tract	Local injection	200 – 300 mL of diluted PROVEDYE® solution in isotonic saline solution
	Ureter leaks and anastomosis visualisation during colorectal or vascular surgery	Local retrograde injection via a urinary catheter	Diluted PROVEDYE® solution in isotonic saline solution
OTHER SURGERY	**Pilonidal sinus visualisation**	Local injection into the pilonidal sinus	2 to 4 mL of solution of PROVEDYE® undiluted or diluted in isotonic saline solution
	Cysts delineation	Local injection directly into the cyst	0.1 to 0.5 mL of undiluted PROVEDYE® solution
	Bladder leaks visualisation	Local injection via a urinary catheter (Foley)	200 – 300 mL of diluted PROVEDYE® solution in isotonic saline solution
	Visualisation of sentinel lymph nodes in melanoma	Peritumoral, intradermal injection	Less than 1 mL of 1.25 mg/mL or 2.5 mg/mL solution of PROVEDYE® in isotonic saline solution

WARNINGS AND PRECAUTIONS:

- PROVEDYE® must be administered 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 PROVEDYE® 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, 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: haemolysis (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).
- Central 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, necrosis (resulting from high doses, if not adequately diluted).
- 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.

Note to the user

Any serious incident that has occurred in relation to the device should be reported to the manufacturer at safety@provepharm.com and the competent authority of the Member State in which the user is established.

SHELF-LIFE

36 months

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 4 - Last revision: 12/2022.

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

ProveDye®

Methylene Blue 0,5%

SPECIAL PRECAUTIONS FOR USE

(Document to keep in the operative theatre)

PROVEDYE® 0.5% sterile solution

Preparation for local or oral administration. Do not inject PROVEDYE® intravenously, intrathecally, intra-amniotically or intraocularly.

PROVEDYE® may be diluted in water (for oral use only), or in isotonic saline solution.

PROVEDYE® must be used immediately after opening or dilution.

PROVEDYE® can be diluted until 0.01%. For example: for a 0.01% dilution, dilute 2 parts of PROVEDYE® 0.5% with 100 parts of isotonic saline solution or water; for a 1.25 mg/mL dilution in isotonic saline solution, dilute 1 part of PROVEDYE® 0.5% with 3 parts of isotonic saline solution.

Any unused product or waste material should be disposed of in accordance with local requirements.

PROVEDYE®	USE	METHOD OF ADMINISTRATION (Proposed route of administration and dilution)	
GASTRO-DIGESTIVE SURGERY	**Colon & bile leakage visualisation**	Local injection via a catheter	1 to 20 mL of a diluted PROVEDYE® solution in isotonic saline solution
	Gastric & pancreatic leakage visualisation	Oral administration or via nasogastric tube	Diluted PROVEDYE® solution in water for injection
	Intra-operative delineation of anal fistula tract	Local injection directly in the external opening	Undiluted PROVEDYE® solution
ENT-ENDOCRINE SURGERY	**Visualisation of sentinel lymph nodes in thyroid cancer**	Peritumoral injection	Up to 0.5 mL diluted PROVEDYE® solution in isotonic saline solution
	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 via endotracheal tube or oesophageal catheter	Diluted PROVEDYE® solution in water for injection
	Intra-operative delineation of tracheo-oesophageal fistula tract		

Instructions for use

ProveDye®
Methylene Blue 0,5%

EN

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

INDICATIONS:
Marker for surgical visualisation such as intra operative seal tests, leakages visualisation and delineation of the fistula tract.

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.

METHOD OF ADMINISTRATION AND DOSAGE:
The PROVEDYE® 0.5% Methylene Blue sterile solution can be administered:
- Undiluted 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 colouration. 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

CE 2797 STERILE 2 STERILIZE 8° C

Provepharm
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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
	Visualisation 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

Provepharm
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WARNINGS AND PRECAUTIONS:

> PROVEDYE® must be administered 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 lose 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 discolouration, 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.
> Ophthalmic: 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.

Note to the user

Any serious incident that has occurred in relation to the device should be reported to the manufacturer (safety@provepharm.com) and the competent authority of the Member State in which the user is established.

SHELF-LIFE:
36 months

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 3 - Last revision : 09/2021

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%. 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		

Provepharm
Life Solutions

28062417

Previous Version 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.

CE 2797 STERILE 8° C 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%. 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

Provepharm Life Solutions

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

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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	
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

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.

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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%. 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.

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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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