Previous Versions Product Information

EN – Instructions for use

ProveDye®
Methylene Blue 0,5%

COMPOSITION:
Each ampoule of PROVEDYE® 0.5% sterile solution contains 10 mg of Methylene Blue (Proveblue®) diluted in 2 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:

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

PUBLICATION DATE :

IFU version 17 - 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 10 mg of Methylene Blue (Proveblue®) diluted in 2 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:

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

PUBLICATION DATE :

IFU version 16 - 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		

Instruction for use

ProveDye® Methylene Blue 0,5%

28063996

EN

COMPOSITION:
Each ampoule of PROVEDYE® 0.5% contains 10 mg of **Methylene Blue (Proveblue®)** diluted in 2 ml of water for injection.

INDICATIONS:
Marker for surgical visualisation such as intra operative seal tests, leakage 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 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

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.

CE 2797 STERILE 2 STERILIZE 8° C

Provepharm Life Solutions

ProveDye® Methylene Blue 0,5%

SPECIAL PRECAUTIONS FOR USE
(to keep in the operative theatre)

PROVEDYE® 0.5% 2 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 DEPART-MENTS	**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-GYNE-COLOGICAL 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 Life Solutions

> 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 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.

Note to the user

Any serious incident that has occured 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:

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

PUBLICATION DATE:

IFU version 15 - 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% 2 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

Instruction for use

ProveDye®
Methylene Blue 0,5%

COMPOSITION:
Each ampoule of PROVEDYE® 0.5% contains 10 mg of **Methylene Blue (Proveblue®)** diluted in 2 ml of water for injection.

INDICATIONS:
Marker for surgical visualisation such as intra operative seal tests, leakage 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 STERILIZE 8° C

Provepharm
Life Solutions

SPECIAL PRECAUTIONS FOR USE

ProveDye®
Methylene Blue 0,5%

(to keep in the operative theatre)

PROVEDYE® 0.5% 2 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
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:
2 ml ampoules, in packs of 5 or 20 ampoules.

PUBLICATION DATE :
IFU version 14 - Last revision: 10/2020.

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% 2 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

Instruction for use

ProveDye®
Methylene Blue 0,5%

COMPOSITION:
Each ampoule of PROVEDYE® 0.5% contains 10 mg of **Methylene Blue (Proveblue®)** diluted in 2 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% 2 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

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:
2 ml ampoules, in packs of 5 or 20 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% 2 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		

Provepharm
Life Solutions

Instruction for use

ProveDye®
Methylene Blue 0,5%

COMPOSITION:
Each ampoule of PROVEDYE® contains 10 mg of **Methylene Blue (Proveblue®)** diluted in 2 ml 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 previous or ongoing 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.

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% 2 ml - 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 > Rectourethral fistula detection	> Via an urinary catheter > Into the vagina during a cystoscopy (200 mL of diluted ProveDye®) > Via an urinary catheter > Via an urethral catheter	X		
	> Ureter leakage detection > Vesicourethral anastomosis Detection	> Via a urinary catheter (5 mL of diluted ProveDye® 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) (0,6-6 mL of ProveDye®) > Into the corpora cavernosa via the urethral meatus			X
GASTRO-DIGESTIVE SURGERY	> Anal fistula detection > Colo-vesical fistula detection > Rectourethral fistula detection > Oesophagial fistula detection	> Via an external catheter > Via an urinary catheter > Via an urethral catheter > Via oral administration (4 mL of ProveDye® in 30 mL 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 ProveDye®) > Via a nasogastric tube > Via a catheter (4mL of ProveDye® in 20 mL of normal saline solution) > Local administration and via oesophageal catheter (4-40 mL of ProveDye® diluted in 20-1000 mL of water or normal saline solution)		X	

Provepharm
Life Solutions

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.
Protective measures against exposure to strong light, including that within instruments such as pulse oximeters should be taken, because there is a risk of cutaneous photosensitivity reaction.

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 or freeze.
Keep the ampoule in the original package to protect it from light.

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

PUBLICATION DATE :
Last revision : 01-2019.

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

Provepharm Life Solutions

Instruction for use

ProveDye® 0,5%
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 previous or ongoing 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 Glu cose-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 • Rectourethral fistula detection	➢ Via an urinary catheter ➢ Into the vagina during a cystoscopy (200 mL of diluted ProveDye®) ➢ Via an urinary catheter ➢ Via an urethral catheter	X		
	• Ureter leakage detection • Vesicourethral anastomosis detection	➢ Via a urinary catheter (5 mL of diluted ProveDye® 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) (0.6-6 mL of ProveDye®) ➢ Into the corpora cavernosa via the urethral meatus			X
GASTRO-DIGESTIVE SURGERY	• Anal fistula detection • Colo-vesical fistula detection • Rectourethral fistula detection • Oesophagial fistula detection	➢ Via an external catheter ➢ Via an urinary catheter ➢ Via an urethral catheter ➢ Via oral administration (4 mL of ProveDye® in 30 mL of water)	X		
	• Colon leakage detection • Gastric leakage detection • Bile leakage detection • Pancreatic leakage detection • Esophagus and lung leakage detection	➢ Via a rectal catheter (1000 mL of normal saline solution containing 20 mL of ProveDye®) ➢ Via a nasogastric tube ➢ Via a catheter (4 mL of ProveDye® in 20 mL of normal saline solution) ➢ Local administration and via oesophageal catheter (4-40 mL of ProveDye® diluted in 20-1000 mL 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.
Protective measures against exposure to strong light, including that within instruments such as pulse oxymeters should be taken, because there is a risk of cutaneous photosensitivity reaction.

ADVERSE EFFECTS:

- Gastrointestinal: nausea, vomiting, diarrhea, abdominal pain, blue colour of faeces and saliva.
- Hematologic: hemolysis (in glucose-6-phosphate dehydrogenase defi ciency, 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 or freeze.
Keep the ampoule in the original package to protect it from light.

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

PUBLICATION DATE :
Last revision : 11-2018.

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) 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
GENERAL SURGERY	• Delineation of cysts	➢ Directly into the cyst (0,2 mL of ProveDye®)			X
BREAST SURGERY	• Visualisation aid during transaxillar en-doscopy • Visualization aid for nipple discharge	➢ At the infra-mammary fold (1-2 mL of ProveDye®) ➢ Directly into the breast duct (2-6 mL of ProveDye®)			X
ENDOCRINE SURGERY	• Identification of the parathyroid glands, re-current nerves and inferior thyroid arteries	➢ Local administration (1 mL of ProveDye®)			X
ENT SURGERY	• Preauricular sinuses (PAS) and branchial sinuses fistula (BSF) detection • Tracheoesophageal/Esophagorespiratory fistulae detection	➢ (2-6 mL of ProveDye®) ➢ Via an endotracheal tube during a bronchoscopy	X		
	• Stain of temporalis fascia graft	➢ Directly into the graft (2 mL of ProveDye®)			X

Previous Version Product Information

Instruction for use

ProveDye® 0,5%
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 orifi ces.
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 • Rectourethral 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 • Rectourethral fi stula 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	

Previous Version Product Information

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 defi ciency, 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 fl uid), 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 infl ammatory 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
Life Solutions

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

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
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

Instruction for use

ProveDye® 0,5%
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 sodium chloride (NaCl) 0.9% solution and must be used immediately after dilution.
PROVEDYE® can also be administered orally after dilution in water.
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 orifi ces.

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 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	➢ Via an urinary catheter ➢ Into the vagina during a cystoscopy (200mL of diluted Methylene Blue)	X		
	• Colo-vesical fistula detection • Rectourethral fistula detection	➢ Via an urinary catheter ➢ Via an urethral catheter			
	• 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	➢ In hydrocele (between tunica vaginalis and albugina) (0.6-6mL of Methylene Blue)			X
	• Localization aid of tunical and urethral tears in corpora cavernosa	➢ Into the corpora cavernosa via the urethral meatus			
GASTRO-DIGESTIVE SURGERY	• Anal fistula detection • Colo-vesical fistula detection • Rectourethral fi stula 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	➢ Via a rectal catheter (1000mL of normal saline solution containing 20mL of Methylene Blue)			
	• Gastric leakage detection • Bile leakage detection	➢ Via a nasogastric tube ➢ Via a catheter (4mL of Methylene Blue in 20 mL of normal saline solution)		X	
	• Pancreatic leakage detection • Esophagus and lung leakage detection	➢ Local administration and via oesophageal catheter (4-40mL of Methylene Blue diluted in 20-1000mL of water or normal saline solution)			

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 defi ciency, 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 fl uid), 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 infl ammatory 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 : 07-2017.

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

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
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

Previous Version Product Information

Instruction for use

ProveDye® 0,5%

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 defi ciency.

In case of moderate or severe renal disease patients must be closely monitored.

ProVepharm Provence Technologies Group 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). 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
URO-GYNECO SURGERY	• Ureterovesical fistula detection • Vesicovaginal fistula detection	➢ Via an urinary catheter ➢ Into the vagina during a cystoscopy (200mL of diluted Methylene Blue)	X		
	• Colo-vesical fistula detection • Rectouretrhal fistula detection	➢ Via an urinary catheter ➢ Via an urethral catheter			
	• 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	➢ In hydrocele (between tunica vaginalis and albugina) (0.6-6mL of Methylene Blue)			X
	• Localization aid of tunical and urethral tears in corpora cavernosa	➢ Into the corpora cavernosa via the urethral meatus			
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	➢ Via a rectal catheter (1000mL of normal saline solution containing 20mL of Methylene Blue)		X	
	• Gastric leakage detection • Bile leakage detection	➢ Via a nasogastric tube ➢ Via a catheter (4mL of Methylene Blue in 20 mL of normal saline solution)			
	• Pancreatic leakage detection • Esophagus and lung leakage detection	➢ Local administration and via oesophageal catheter (4-40mL of Methylene Blue diluted in 20-1000mL of water or normal saline solution)			

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 : 09-2016.

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

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	FIS-TULA	LEAK-AGE	DELIN-EATION
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

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 Provence Technologies Group CE 0086 STERILE

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

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 of decrease of technical performance such as contamination.
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. Eye: 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 : 05-2016.

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

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	√ At the infra-mammary fold (1-2mL of Methylene Blue)			x
	• Visualisation aid for nipple discharge	√ Directly into the breast duct (2-6mL of Methylene Blue)			
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	√ (2-6mL of Methylene Blue)			
	• Tracheoesophageal/Esophagorespiratory fistulae detection	√ Via an endotracheal tube during a bronchoscopy	x		
	• Stain of temporalis fascia graft	√ Directly into the graft (2mL of Methylene Blue)			x

PROVEDYE® 0,5% Leaflet

Composition:
Each ampoule of PROVEDYE® contains 10 mg of Methylene Blue (Proveblue®) diluted in 2 ml of water solution for injection.

Indications:
Visualization aid for surgical procedures such as the delineation of tissues and operative pieces, seal test for sutures, detection of leaks, fistula detection.

Contraindications
Do not administrate PROVEDYE®:
- In case of known hypersensitivity to 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 the case of Glucose-6-Phosphate Dehydrogenase deficiency.

In the case of moderate or severe renal disease the patient must be closely monitored.

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 administered 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.

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.
- Nervous system: headaches, dizziness, mental confusion, anxiety, tremor, fever, aphasia, agitation.
- Administration site : thrombophlebitis (resulting from high doses, if not adequatly diluted - not more than 350 mg of methylene blue should be diluted in each 500 ml of fluid infusion), necrosis (if extravasation occurs).

Previous Version Product Information

- Renal: blue color of the urine.
- Respiratory, thoracic and mediastinal: dyspnea, tachypnea, hypoxia.
- Ophtalmologic: eye 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.

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 of decrease of technical performance due to contamination.
PROVEDYE® should be disposed of in clinical waste.

Precautions for use
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.

Storage
Do not refrigerate PROVEDYE® under 8°C or freeze.
Keep the ampoule in the original packaging to protect it from light.

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

Publication date:

Last revision: 11/2015

CE 0086 STERILE 2 STERILIZE 8°C

Provepharm
Provence Technologies Group

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

SPECIAL PRECAUTIONS FOR USE (to keep in the operating room)

PROVEDYE® 0.5% 2ml – Sterile solution

Preparation for local or oral administration
Do not inject PROVEDYE® in an 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.

CE 0086 STERILE 2 STERILIZE 8°C

Provepharm
Provence Technologies Group

ProveDye® METHYLENE BLUE **0.5%**

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 the delineation of tissues and operative pieces, Seal test for sutures, detection of leaks, fistula detection.

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.

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 epithelium of the organ via the existing natural orifices. PROVEDYE® can also be administered orally after 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. Eye: 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.

Warnings
•Do not inject PROVEDYE® intravenously, subcutaneously, intrathecally and intra-amniotically
•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 of decrease of technical performance such as contamination
•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

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: 08-2015

CE 0086 8°C STERILIZE STERILE

ProVepharm PROVENCE TECHNOLOGIES GROUP

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

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 and intra-amniotic 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.

CE 0086 8°C STERILIZE STERILE

ProVepharm PROVENCE TECHNOLOGIES GROUP

PROVEDYE™ 0.5% Leaflet

ProveDye™
METHYLENE BLUE

Composition:
Each ampoule of PROVEDYE™ contains 10 mg of methylene blue (Proveblue®) diluted in 2 ml of water solution for injection.

Indications:
Visualization aid for surgical procedures such as the delineation of tissues and operative pieces, seal test for sutures, detection of leaks, fistula detection.

Contraindications
Do not administrate PROVEDYE™ :
- In case of known hypersensitivity to methylene blue or to any other thiazine dyes;
- In case of treatment with selective serotonin reuptake inhibitors (SSRI), bupropion, buspirone, clomipramine, mirtazapine and venlafaxine;
- In case of pregnancy or breastfeeding, PROVEDYE™ should be avoided;
- In the case of Glucose-6-Phosphate Dehydrogenase deficiency.

In the case of moderate or severe renal disease the patient must be closely monitored.

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 administered 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.

Adverse effects
- Gastrointestinal: nausea, vomiting, diarrhea, abdominal pain, blue colour of faeces and saliva.
- Hematology: 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.
- Nervous system: headaches, dizziness, mental confusion, anxiety, tremor, fever, aphasia, agitation.
- Injection site : thrombophlebitis (resulting from high doses, if not adequatly diluted - not more than 350 mg of methylene blue should be diluted in each 500 ml of fluid infusion), necrosis (if extravasation occurs).

Previous Version Product Information

- Renal: blue color of the urine.
- Respiratory, thoracic and mediastinal disorders: dyspnea, tachypnea, hypoxia.
- Ophthalmology: eye 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.

Warnings
Do not inject PROVEDYE™ intravenously, subcutaneously, intrathecally and intra-amniotically.
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.
PROVEDYE™ should be disposed of in clinical waste.
In case of re-use of PROVEDYE™ , there is a risk of decrease of technical performance such as contamination.
Follow the risk management plan for the operative theatre.
Keep out of reach of children.

Precautions for use
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.

Storage
Do not refrigerate PROVEDYE™ under 8°C or freeze.
Keep the ampoule in the original packaging to protect it from light.

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

Publication date:
Last revision: 10 2014

CE 0086 STERILE 2 STERILIZE 8°C

ProVepharm
PROVENCE TECHNOLOGIES GROUP

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

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SPECIAL PRECAUTIONS FOR USE (to be kept in the operating theatre)

PROVEDYE™ 0.5% 2ml – Sterile solution

Preparation for local administration
Do not inject PROVEDYE™ in an intravenous, subcutaneous, intrathecal or intra-amniotic 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 should be disposed of in accordance with local requirements.

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ProVepharm
PROVENCE TECHNOLOGIES GROUP

ProveDye™ METHYLENE BLUE **0.5%**

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 the delineation of tissues and operative pieces, Seal test for sutures, detection of leaks, fistula detection.

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.

Method of administration and dosage
A preoperative assessment is recommended before using PROVEDYE®. PROVEDYE® water (for oral use only). PROVEDYE® may be diluted 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 epithelium of the organ via the existing natural orifices. PROVEDYE® can also be administered orally after 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.
• Injection 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. Eye: 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.

Warnings
•Do not inject Provedye® intravenously, subcutaneously, intrathecally and intra-amniotically
•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 of decrease of technical performance such as contamination
•Provedye® should be disposed of in clinical waste.
•Follow the Risk management Plan for operative theatre;
•Keep out of reach of children.

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

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: 10-2014

CE 0086 8°C 2 STERILIZE STERILE

ProVepharm PROVENCE TECHNOLOGIES GROUP

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

SPECIAL PRECAUTIONS FOR USE *(to keep in the operative theatre)*
PROVEDYE® 0.5% 2ml – Sterile solution
ProveDye™ METHYLENE BLUE
Preparation for Local administration.
Do not inject PROVEDYE® in Intravenous, subcutaneous, intrathecal and intra-amniotic injection
PROVEDYE® may be diluted 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 administred 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.

CE 0086 8°C 2 STERILIZE STERILE

ProVepharm PROVENCE TECHNOLOGIES GROUP

ProveDye™ METHYLENE BLUE **0.5%**

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 the delineation of tissues and operative pieces, Seal test for sutures, detection of leaks, fistula detection.

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.

Method of administration and dosage
A preoperative assessment is recommended before using PROVEDYE®. PROVEDYE® may be diluted in a Glucose 5% solution or in a sterile water solution. The PROVEDYE® dilution and volume to be administrated depends on the destination and size of the area to be coloured. PROVEDYE® could be diluted between 0.01% and 0.5%. 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 epithelium of the organ via the existing natural orifices. PROVEDYE® can also be administered orally after 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.
• Injection 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. Eye: 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.

Warnings
•Do not inject Provedye® intravenously, subcutaneously, intrathecally and intra-amniotically
•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 of decrease of technical performance such as contamination
•Provedye® should be disposed of in clinical waste.
•Follow the Risk management Plan for operative theatre;
•Keep out of reach of children.

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
•PROVEDYE® should not be diluted with sodium chloride Solution (NaCl).

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: 09-2014

CE 0086 8°C

Provepharm PROVENCE TECHNOLOGIES GROUP STERILE

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

SPECIAL PRECAUTIONS FOR USE *(to keep in the operative theatre)*
PROVEDYE® 0.5% 2ml – Sterile solution
Preparation for Local administration.
Do not inject PROVEDYE® in Intravenous, subcutaneous, intrathecal and intra-amniotic injection
PROVEDYE® may be diluted in 50 ml glucose 50 mg/ml (5%) solution or in a sterile water solution for injection.
PROVEDYE® must not be diluted with sodium chloride (NaCl) solution for injection because it has been demonstrated that chloride reduces the solubility of Methylene Blue 0.5%. PROVEDYE® could be diluted between 0.01% and 0.5%.
Additional information on the way in which PROVEDYE® can be administred 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.

CE 0086 8°C STERILE

Previous Version Product Information

ProveDye™ METHYLENE BLUE **0.5%**

Composition:

Each ampoule of PROVEDYE® contains 10mg of Methylene Blue (Proveblue®) diluted in 2ml of water for injection.

Indications:

Visualization aid for surgical procedures such as the delineation of tissues and operative pieces, Seal test for sutures, detection of leaks, fistula detection.

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 should be closely monitored.

Mode of administration and dosage

A preoperative assessment is recommended before using PROVEDYE®.

PROVEDYE® may be diluted in Glucose 5% solution for injection or sterile water solution.
The dilution of PROVEDYE® and the volume to administrate depend of the staining destination and the size of the zone to stain.
PROVEDYE® may be deposited in contact with the anatomic structure after dilution.
PROVEDYE® can also be injected in the light of some organs, or put in contact with the epithelium of the organ through natural existing orifice.
PROVEDYE® can also be administered orally after dilution.

Side 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.
- Injection 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. Eye: 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.

Warnings

Do not injected PROVEDYE® in Intravenous, subcutaneous, intrathecal and intra-amniotic injection
Do not use PROVEDYE® if the solution is colourless;
Do not use a damaged ampoule of PROVEDYE®.

PROVEDYE® is for single use only: Throw any remaining solution after opening.
PROVEDYE® should be eliminate throw hospital waste.
Follow the Risk management Plan for operative room.
Keep out of the reach of children

Precautions

PROVEDYE® must be used by a healthcare professional.
Gloves are recommended for users.
PROVEDYE® must be used immediately after opening or dilution
PROVEDYE® should not be diluted with NaCl Solution for injection.

Storage

Do not refrigerate PROVEDYE® under 8°C or freeze.
Keep the ampoule in the original package in order to protect from light.

Conditioning:

2ml ampoules, in packs of 5 or 20 ampoules

Publication date

Last revision: 07-2014

CE 0086 (MM YYYY)

STERILE A

8°C

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

Previous Version Product Information

SPECIAL PRECAUTIONS FOR USE *(to keep in the operative theatre)*

PROVEDYE® 0.5% 2ml – Sterile solution

Preparation for Local administration.
Do not inject PROVEDYE® in Intravenous, subcutaneous, intrathecal and intra-amniotic injection
PROVEDYE® may be diluted in 50 ml glucose 50 mg/ml (5%) solution for injection or water sterile solution.
PROVEDYE® must not be diluted with sodium chloride (NaCl) solution for injection because it has been demonstrated that chloride reduces the solubility of Methylene Blue 0.5%.
Additional information on how PROVEDYE® can be given is provided in the Instructions for use.
Use immediately on opening. Any unused product or waste material should be disposed of in accordance with local requirements.

0086 (MM YYYY)

8°C
