

## **PRODUCT MONOGRAPH**

METHYLENE BLUE INJECTION USP

1% w / v (10 mg / mL)

Sterile solution

Intravenous

**METHEMOGLOBINEMIA / DIAGNOSTIC AID**

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## **METHYLENE BLUE INJECTION USP**

(Tetramethylthionine Chloride Trihydrate)

### **THERAPEUTIC CATEGORY: METHEMOGLOBINEMIA/DIAGNOSTIC AID**

Recent research has revealed that methylene blue has structural properties similar to Monoamine oxidase inhibitors (MAOI), known precipitants of serotonin toxicity when administered concomitantly with drugs having serotonin reuptake inhibition properties (SRIs). Serotonin toxicity/serotonin syndrome has been reported when methylene blue was administered intravenously at concentrations as low as 1 mg/kg, in patients receiving Selective Serotonine Reuptake Inhibitors (SSRIs) or other drugs with serotonine reuptake inhibition properties (e.g.: duloxetine, venlafaxine and clomipramine). Several of these cases required admission to Intensive Care Unit.

If SRIs are being taken, careful consideration needs to be given to stop them before methylene blue injectable use to allow a washout period equivalent to at least 4-5 half-lives.

### **ACTION AND PHARMACOLOGY:**

Methylene blue activates a normally dormant reductase enzyme system which reduces the methylene blue to leucomethylene blue, which in turns is able to reduce methemoglobin to hemoglobin. Methylene blue is absorbed from the gastro-intestinal tract. It is believed to be reduced in the tissues to the leuco form which is slowly excreted, mainly in the urine together with some unchanged drug. Methylene blue imparts a blue colour to urine and feces. In large doses methylene blue can produce methemoglobinemia.

### **INDICATIONS AND CLINICAL USE:**

Methylene Blue Injection USP is used in the treatment of methemoglobinemia. Methylene Blue Injection USP is also used as bacteriological stain, as a dye in diagnostic procedures such as fistula detection, and for the delineation of certain body tissues during surgery.

**CONTRAINDICATIONS:**

Methylene Blue Injection USP is contraindicated in patients with severe renal impairment or a known hypersensitivity to the drug.

**PRECAUTIONS:**

Methemoglobin concentration should be closely monitored during treatment as methylene blue can produce methemoglobinemia in large doses.

For management of a suspected drug overdose, contact your regional Poison Control Centre immediately.

Methylene Blue Injection USP should be used with caution in the treatment of toxic methemoglobinemia; high doses can cause hemolytic anemias and patients with glucose-6-phosphate dehydrogenase (G6PD) deficiencies are particularly susceptible.

A rapid disappearance of cyanosis in response to Methylene Blue Injection USP would be expected within one hour but might not occur if the patient has erythrocyte G6PD or NADPH-diaphorase deficiency or if methemoglobinemia is due to the ingestion of compounds such as aniline or dapsone. A second dose has been recommended if cyanosis does not disappear within one hour of Methylene Blue Injection USP administration but results of a study in animals and of patient with aniline poisoning indicated that an increased dosage of methylene blue might be of no additional benefit and could be potentially dangerous in that it could enhance Heinz body formation.

Methylene Blue Injection USP should not be injected subcutaneously as it may cause necrotic abscesses. It should not be given by intrathecal injection as neural damage has occurred.

Methylene Blue Injection USP should be used with caution in patients with glucose-6-phosphate dehydrogenase deficiency.

**PREGNANCY AND LACTATION:**

Although intra-amniotic injection of methylene blue has been used to diagnose premature rupture of fetal membranes or to identify separate amniotic sacs in twin pregnancies, there have been several reports of hemolytic anemia (Heinz-body anemia) and hyperbilirubinemia in neonates

exposed to methylene blue in the amniotic cavity. In most cases, exchanges transfusions, and/or phototherapy are required to control the jaundice.

**ADVERSE REACTIONS:**

After intravenous administration Methylene Blue Injection USP may cause nausea, vomiting, abdominal and chest pain, headache, dizziness, mental confusion, profuse sweating, and hypertension, with very high doses, methemoglobinemia and hemolysis may occur.

**DOSAGE AND ADMINISTRATION:**

As a methoglobinemic: For the treatment of drug induced methemoglobinemia as in nitrite poisoning. Methylene Blue Injection USP is administered intravenously as a 1% solution in doses of 1 to 2 mg/kg body weight injected over a period of several minutes. A repeat dose may be given after one hour if required.

As a diagnostic aid: For the detection of fistulas, 1 to 3 mL of Methylene Blue Injection USP is injected into the opening and the appearance of blue discoloration is observed in the surrounding tissue.

**AVAILABILITY:**

Each mL of sterile solution contains 10 mg of methylene blue (Tetramethylthionine chloride Trihydrate) in water for injection. Also contains sodium hydroxide and hydrochloric acid to adjust pH.

Ampoules of 5 mL, boxes of 5. Store at room temperature (15 to 30°C).

**Reporting Side Effects**

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

*NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.*

**Questions or concerns?**

Contact Hikma Canada Limited at 1-800-656-0793

This leaflet was prepared by Hikma Canada Limited, Mississauga, ON L5R 3P9

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**REFERENCE:**

Bioniche Pharma (Canada) Ltd, Prescribing Information, Methylene Blue Injection USP, DIN 02094665, February 22, 2011.