METHYLENE BLUE- methylene blue injection
BPI LABS LLC

Disclaimer: This drug has not been found by FDA to be safe and effective, and this labeling has not been approved by FDA. For further information about unapproved drugs, click here.

Methylene Blue Injection 1%

(FOR SLOW INTRAVENOUS ADMINISTRATION)

Rx only

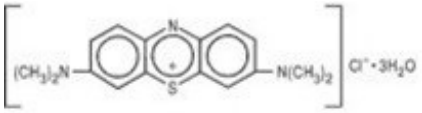
WARNING: SEROTONIN SYNDROME WITH CONCOMITANT USE OF SEROTONERGIC DRUGS

Methylene Blue Injection may cause serious or fatal serotonergic syndrome when used in combination with serotonergic drugs. Avoid concomitant use of Methylene Blue Injection with selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), and monoamine oxidase inhibitors (see WARNINGS and PRECAUTIONS, Drug Interactions).

DESCRIPTION

Methylene Blue Injection is a sterile solution of Phenothiazin-5-ium, 3, 7-bis (dimethylamino)-, chloride, trihydrate. Each mL contains methylene blue, 10 mg in water for injection q.s. pH adjusted with sodium hydroxide and/or hydrochloric acid when necessary.

The structural formula is:



The molecular formula is:

C16H18ClN3S • 3H2O MW = 373.90

CLINICAL PHARMACOLOGY

Methylene blue will produce two opposite actions on hemoglobin. Low concentrations will convert methemoglobin to hemoglobin. High concentrations convert the ferrous iron of reduced hemoglobin to ferric iron which results in the formation of methemoglobin.

Methylene blue is metabolized in the body to leukomethylene blue which is excreted primarily in the urine. Some unchanged drug is also excreted in the urine. (1)

INDICATIONS AND USAGE

Drug-induced methemoglobinemia

CONTRAINDICATIONS

Methylene blue can cause fetal harm when administered to a pregnant woman. An association exists between the use of methylene blue in amniocentesis and atresia of the ileum and jejunum, ileal occlusions, and other adverse effects in the neonate. (2, 3) Methylene blue is contraindicated in women who are or may become pregnant. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

Intraspinal and subcutaneous injections are contraindicated.

Methylene blue is contraindicated in patients with a known hypersensitivity to the drug.

WARNINGS

Methylene blue should not be given by subcutaneous or intrathecal injection.

Methylene blue is a potent monoamine oxidase inhibitor: Methylene blue has been demonstrated to be a potent monoamine oxidase inhibitor (MAOI) and may cause potentially fatal serotonin toxicity (serotonin syndrome) when combined with serotonin reuptake inhibitors (SRIs). (4) (see **DRUG INTERACTIONS**.) Serotonin toxicity is characterized by development of neuromuscular hyperactivity (tremor, clonus, myoclonus, and hyperreflexia, and, in the advanced stage, pyramidal rigidity); autonomic hyperactivity (diaphoresis, fever, tachycardia, tachypnoea, and mydriasis); and altered mental status (agitation, excitement, and in the advanced stage, confusion). If methylene blue is judged to be indicated, SRIs must be ceased, prior to treatment/procedure/surgery.

PRECAUTIONS

Drug Interactions: Methylene blue may interact with any drug that acts as a serotonin reuptake inhibitor (SRI) including, amongst others, selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), norepinephrine-dopamine reuptake inhibitors (NDRIs), triptans and ergot alkaloids; such combinations may have the consequence of potentially fatal serotonin toxicity (serotonin syndrome). Methylene blue should not be co- administered with any drug that acts as an SRI.

Pregnancy: Pregnancy Category X: Epidemiologic evidence exists that methylene blue is a teratogen. An association exists between the use of methylene blue in amniocentesis and atresia of the ileum and jejunum, ileal occlusions, and other adverse effects in the neonate. (2,3) Methylene blue injection should not be administered to pregnant women during amniocentesis due to the risk of teratogenicity and other newborn adverse effects (see **CONTRAINDICATIONS**).

Glucose-6-Phosphate Dehydrogenase Deficiency (G6PD Deficiency): Methylene blue should be avoided in patients with G6PD deficiency due to the risk of paradoxical methemoglobinemia and hemolysis. (5,6)

Renal Failure: Methylene blue should be used with caution in patients with severe renal

impairment (see **CLINICAL PHARMACOLOGY**).

Methylene blue must be injected intravenously very slowly over a period of several minutes to prevent local high concentration of the compound from producing additional methemoglobin. Do not exceed recommended dosage.

Large intravenous doses of methylene blue produce nausea, abdominal and precordial pain, dizziness, headache, profuse sweating, mental confusion, and the formation of methemoglobin.

DOSAGE AND ADMINISTRATION

0.1 to 0.2 mL per kg body weight (0.045 to 0.09 mL per pound body weight). Inject methylene blue intravenously very slowly over a period of several minutes.

Methylene blue must be injected intravenously very slowly over a period of several minutes to prevent local high concentration of the compound from producing additional methemoglobin. Do not exceed recommended dosage. Parenteral drug products should be inspected visually for particulate matter and discoloration, whenever solution and container permit.

HOW SUPPLIED

Methylene Blue Injection, 1% is supplied as follows:

NDC 54288-147-01

10 mL single dose vial per carton.

To report SUSPECTED ADVERSE REACTIONS, contact BPI Labs LLC at 727-471-0850 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

STORAGE

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

REFERENCES

1. DiSanto AR, Wagner JG. Pharmacokinetics of highly ionized drugs II: methylene blue – absorption, metabolism, and excretion in man and dog after oral administration. J Pharm Sci. 1972; 61:1086- 1090.
2. Cragan JD. Teratogen update: methylene blue. Teratology. 1999; 60:42-48.
3. Kidd SA, Lancaster PA, Anderson JC, Boogert A, Fisher CC, Robertson R, et al. Fetal death after exposure to methylene blue dye during mid-trimester amniocentesis in twin pregnancy. Prenat Diagn. 1996; 16:39-47.
4. Ramsay RR, Dunford C, Gillman PK. Methylene blue and serotonin toxicity: inhibition of monoamine oxidase A (MAOA) confirms a theoretical prediction. Br J Pharmacol. 2007; 152:946-51.
5. Beutler E. G6PD Deficiency. Blood. 1994; 84:3613-3636.
6. Youngster I, Arcavi L, Schechmaster R, Akayzen Y, Popliski H, Shimonov J, Beig S, Berkovitch M. Medications and glucose-6-phosphate dehydrogenase deficiency: an

evidence-based review. Drug Saf. 2010; 33:713-726.

Manufactured by:

BPI Labs, LLC

12393 Belcher Road S, Suite 450,

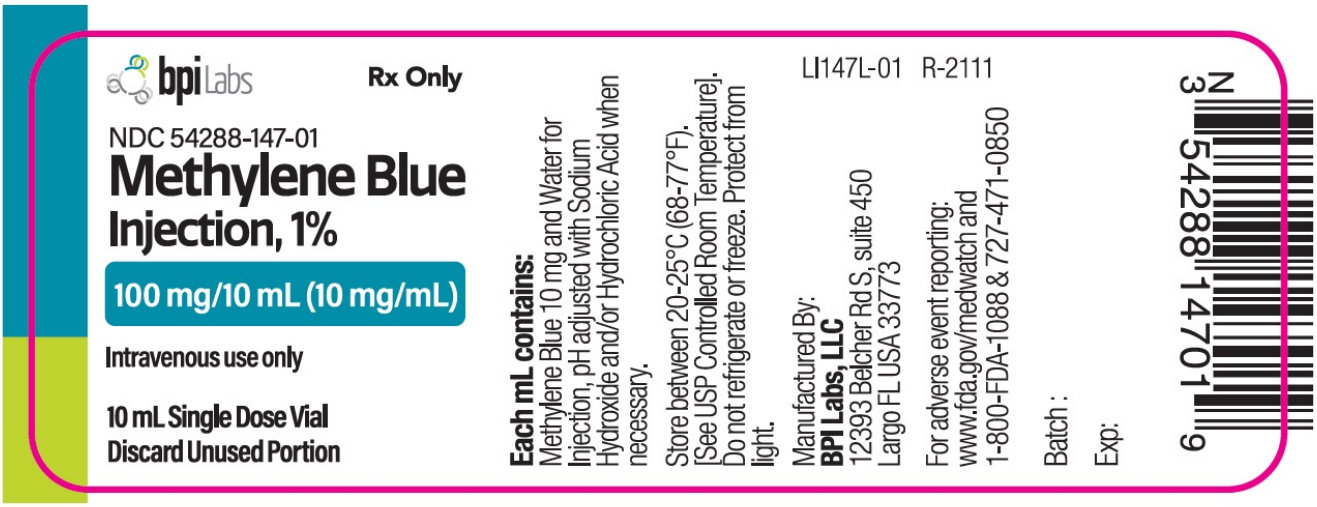
Largo, FL 33773

LI38I

R-2111

PRINCIPAL DISPLAY PANEL


bpi Labs
Rx Only
NDC 54288-147-01
Methylene Blue
Injection, 1%
100 mg/10 mL (10 mg/mL)
Intravenous use only
Each mL contains: Methylene Blue 10 mg and Water for Injection, pH adjusted with Sodium Hydroxide and/or Hydrochloric Acid when necessary.
Store between 20-25°C (68-77°F) [see USP Controlled Room Temperature].
Do not refrigerate or freeze. Protect from light.
For adverse event reporting:
www.fda.gov/medwatch and 1-800-FDA-1088 & 727-471-0850
Manufactured By:
BPI Labs, LLC
12393 Belcher Rd S, suite 450
Largo FL USA 33773
LI147C-01
R-2111
N 3 54288 14701 9
10 mL Single Dose Vial
Discard Unused Portion
NON VARNISH AREA



METHYLENE BLUE

methylene blue injection

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:54288-147
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
METHYLENE BLUE (UNII: T42P99266K) (METHYLENE BLUE CATION - UNII:ZMZ79891ZH)	METHYLENE BLUE	10 mg in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
WATER (UNII: 059QF0KO0R)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
HYDROCHLORIC ACID (UNII: QTT17582CB)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:54288-147-01	10 mL in 1 VIAL; Type 0: Not a Combination Product	12/23/2021	

Marketing Information			
Marketing Category	**Application Number or Monograph Citation**	**Marketing Start Date**	**Marketing End Date**

unapproved drug other		12/23/2021	

Labeler - BPI LABS LLC (078627620)

Establishment

Name	Address	ID/FEI	Business Operations
BPI LABS LLC		078627620	manufacture(54288-147) , label(54288-147)

Revised: 10/2023 BPI LABS LLC