

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

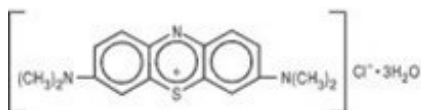
**WARNING: SEROTONIN SYNDROME WITH CONCOMITANT USE OF
SEROTONERGIC DRUGS**

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:

$C_{16}H_{18}ClN_3S \cdot 3H_2O$ 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 54288-159-05

Five 2 mL Single-Dose Prefilled Syringes packed in a 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

LI501

R-2302

PRINCIPAL DISPLAY PANEL

Approx. mg mL

200—20 150—15 100—10 50—0.5

NDC 54288-159-01 Rx Only


Methylene Blue
Injection, 1%

20 mg/2 mL
(10 mg/mL)

2 mL Single-Dose Prefilled Syringe

Intravenous use only


Discard unused portion

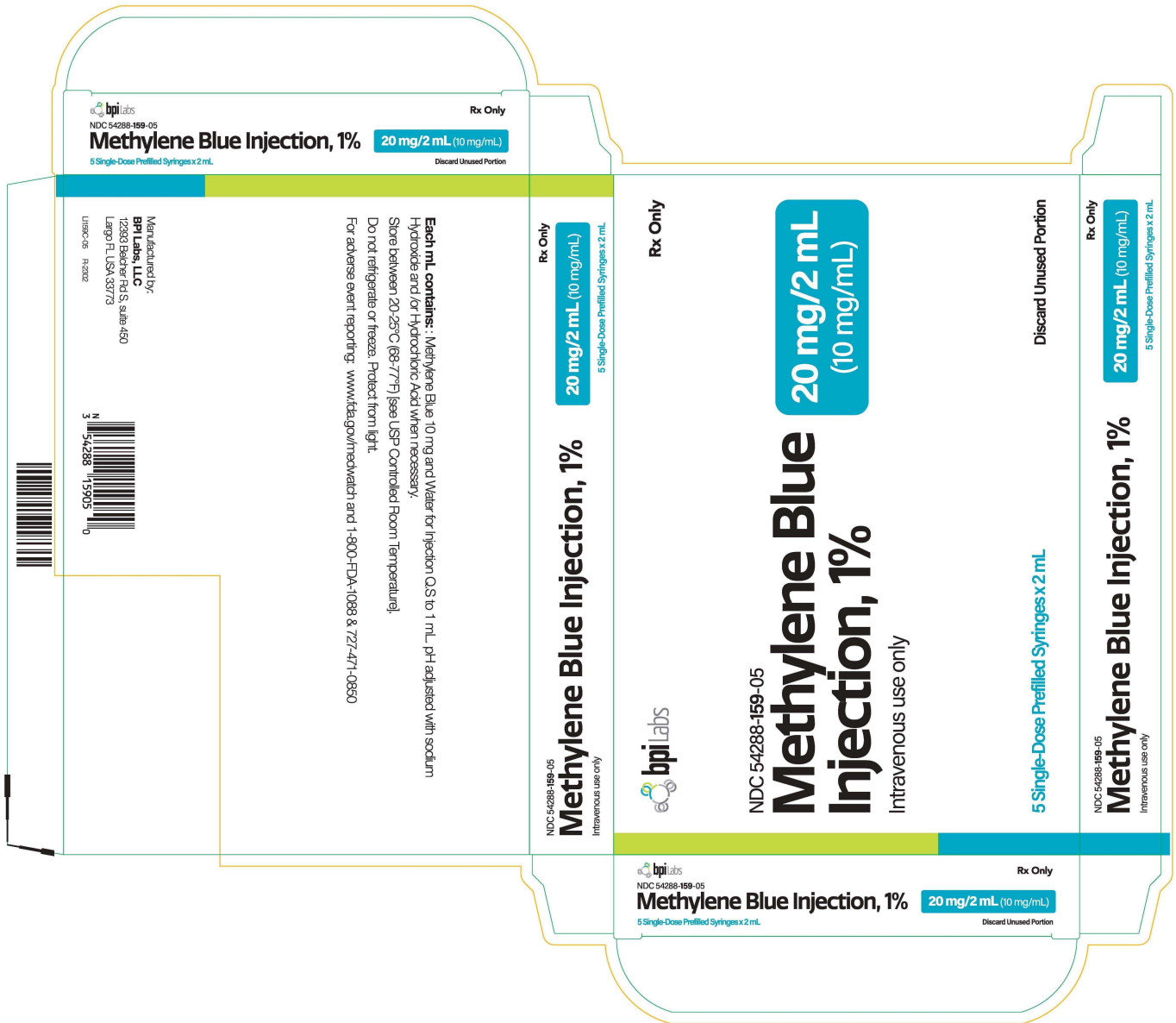


Manufactured By: **BPI Labs, LLC** LI159L-01 R-2212
12393 Belcher Rd S, Suite 450.
Largo, FL USA 33773

Batch:

Exp:

N 3  54288 15901 2



METHYLENE BLUE

methylene blue injection

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:54288-159
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:54288-159-05	5 in 1 PACKAGE	05/15/2023	
1	NDC:54288-159-01	2 mL in 1 SYRINGE; Type 2: Prefilled Drug Delivery Device/System (syringe, patch, etc.)		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
unapproved drug other		05/15/2023	

Labeler - BPI LABS LLC (078627620)

Establishment

Name	Address	ID/FEI	Business Operations
BPI LABS LLC		078627620	analysis(54288-159) , manufacture(54288-159) , label(54288-159)

Revised: 10/2023

BPI LABS LLC