RonanRx
PERSONALIZED MEDICINE

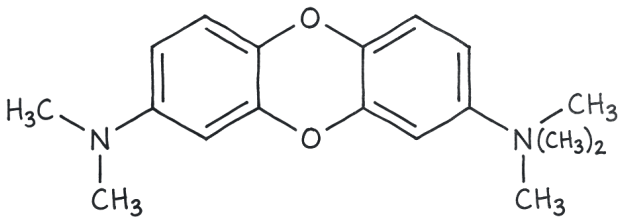
CLINICAL MONOGRAPH · ANTIOXIDANT & MITOCHONDRIAL

Methylene Blue

Thiazine redox agent in sterile injection and custom oral strengths

Methylene blue is a deep-blue medicine that has been used in clinics for more than a century. Its best-established job is as an antidote: in a condition called methemoglobinemia, the iron in your red blood cells gets locked in a form that cannot carry oxygen, and methylene blue flips it back so the blood works again. The FDA-approved injectable version is ProvayBlue, cleared in 2016 for that exact use in adults and children [1].

Doctors also use methylene blue in the hospital for other problems, most notably a dangerous drop in blood pressure that can happen after heart surgery, and to help prevent confusion caused by the chemotherapy drug ifosfamide. RonanRx prepares compounded methylene blue only on a patient-specific prescription, as a sterile injection or a custom low-dose oral form, using pharmaceutical-grade ingredient. It has two safety facts that matter a lot: it must not be combined with common antidepressants because the mix can be dangerous, and it should not be used in people with a genetic condition called G6PD deficiency [17].



EVIDENCE POSTURE FDA APPROVED WELL STUDIED REVIEWED **2026-06-26**

State-licensed 503A | Pharmacist reviewed | Doctor led | Cold-chain ready | Patient choice preserved

Contents

Click any section to jump there. Page numbers update on render.

Why personalized 5
Quick facts 5
How this differs from research-use-only 6
What it is 6
How it works 7
Biological role 7
Detailed mechanism 8
Research history 8
Timeline 9
Clinical contexts studied 10
Off-label uses 12
FDA-approved use 12
Compounded form (503A) 13
Formulations and routes 13
Dosing 14
Safety 15
Monitoring 17
Special populations 17
Evidence quality 17
Major studies 17
Pharmacology (PK/PD) 20
Comparative formulations 21
Storage 21
Compounding & operations 21
FAQ 22

References 23
How to access 26

FOR CLINICIANS

Methylene blue (methylthioninium chloride) is a phenothiazine-derived thiazine dye and redox-active small molecule. Its pharmacology is biphasic and dose-dependent. At low doses it acts as an electron donor and redox cycler, accepting electrons via the NADPH-dependent methemoglobin reductase system and reducing ferric methemoglobin (Fe3+) back to functional ferrous hemoglobin (Fe2+); at high doses it can oxidize hemoglobin and precipitate methemoglobinemia and hemolysis [1110]. It is also a potent inhibitor of monoamine oxidase A and an inhibitor of the nitric oxide and soluble guanylate cyclase pathway, the mechanistic basis for both its serotonin-toxicity risk and its vasopressor-sparing effect in vasoplegia [71314].

The only FDA-approved indication is acquired methemoglobinemia, marketed as ProvayBlue (methylene blue injection, USP; approved 2016), dosed at 1 mg/kg IV over 5 to 30 minutes with a possible repeat dose [1]. Off-label and well-studied hospital uses include refractory vasoplegic syndrome after cardiopulmonary bypass [1821], ifosfamide-induced encephalopathy [16], and refractory septic shock [17]. Methylene blue carries a boxed warning for serotonin syndrome with serotonergic drugs, a contraindication in G6PD deficiency, transient pulse-oximetry interference (falsely low SpO2), blue-green discoloration of urine and stool, and pregnancy caution (intra-amniotic exposure has caused fetal harm) [11920].

RonanRx compounds methylene blue under 503A on patient-specific prescriptions: sterile IV preparations when the manufactured product is not appropriate or available, and custom low-dose oral capsules or solution when a prescriber documents a clinical need that no manufactured product meets. Pharmaceutical (USP) grade ingredient, sterility control for injectables, and lot traceability are the controls that separate a compounded preparation from industrial dye [2830].

Why Personalized Methylene Blue

The injectable methylene blue dose that the FDA reviewed was calibrated for one job: reversing methemoglobinemia at 1 mg/kg in the average adult or child. That single number does not account for the steepest fact about this molecule, that its dose-response runs both ways. A dose that rescues oxygen-carrying capacity at the low end can itself cause methemoglobinemia and red-cell breakdown at the high end, and a strength that is right for an acute antidote is wrong for a quiet low-dose oral use a clinician might want. The manufactured product also assumes the patient is not carrying the two facts that change everything for this drug: a G6PD enzyme deficiency that makes it both useless and dangerous, and a serotonergic antidepressant in their medication list that turns a routine dose into a serotonin-toxicity risk.

A compounding pharmacy is built for exactly those individual variables. A prescriber can order a custom low-dose oral capsule or solution for a patient who needs a measured oral dose rather than the hospital injection, or a sterile injectable strength prepared to the prescribed concentration when the manufactured product is not the right fit, all from pharmaceutical-grade methylthioninium chloride rather than the industrial dye sold online. Just as important, the pharmacy review is the place where the serotonergic-drug check and the G6PD consideration happen before the preparation is dispensed. The molecule is the same redox agent medicine has used for over a century. The strength, the route, and the safety screen are written for one named patient.

This is the older arrangement that pre-dates mass-produced vials. A doctor writes the prescription, a pharmacist prepares it for that patient and puts that patient's name on the label, and modern state-board inspection and 503A oversight keep the work honest.

Quick Facts About Methylene Blue

Category: Thiazine dye and redox (oxidation-reduction) agent; potent monoamine oxidase A inhibitor [57]

Active ingredient: Methylene blue (methylthioninium chloride), USP grade only

Chemistry: CAS 61-73-4; PubChem CID 6099; molecular formula C16H18ClN3S; molecular weight about 319.85 g/mol [3]

FDA-approved branded form: ProvayBlue (methylene blue injection, USP), approved 2016 for acquired methemoglobinemia in adults and children. Long-standing generic methylene blue injection USP is also marketed. [1]

Routes: Intravenous injection (sterile, USP) for methemoglobinemia and acute hospital uses; custom-strength oral capsules or solution (low-dose) when a prescriber documents a clinical need [115]

Dose-dependent behavior: Low doses reduce ferric methemoglobin back to functional hemoglobin; high doses can paradoxically cause methemoglobinemia and hemolysis. The dose right for one indication is wrong for another. [1110]

Critical interaction: Potent MAO-A inhibition means combining methylene blue with serotonergic drugs (SSRIs, SNRIs, MAOIs, and others) can cause serious or fatal serotonin toxicity. Subject of an FDA 2011 Drug Safety Communication and a boxed warning. [127]

Contraindicated: Glucose-6-phosphate dehydrogenase (G6PD) deficiency (risk of severe hemolysis; also ineffective for methemoglobinemia in this population) and severe hypersensitivity. [1]

Compounded under: 503A, patient-specific prescription only, pharmaceutical (USP) grade ingredient. Aquarium-grade or research-chemical methylene blue is not medicine. [28]

SPECIALS: PATIENT-SPECIFIC PRESCRIPTION ONLY

Methylene Blue described in this monograph is a 503A compounded preparation. Every dose is made on a prescription, for a named patient, by a licensed pharmacist. It is not a stocked, mass-manufactured product.

- **Made to order, not off a shelf.** No batch sits in a warehouse waiting for buyers. Your prescription triggers the prep.
- **Named-patient label.** The bottle carries one patient's name. The batch records carry one prescription.
- **Dose, strength, and route chosen for the patient.** A prescriber decides what gets compounded, not a manufacturer who set the strength for a trial population.
- **Licensed pharmacist on the hook.** A real person, with a license that can be pulled, signs off on every prep. State inspectors check the facility.
- **Compounded drugs are not FDA-approved.** They should not be evaluated using branded-drug trial data alone. Availability varies by state and prescribed medication.

How This Differs from a Research-Use-Only Website

A research-use-only website ships a vial from a warehouse. There is no prescription, no pharmacist, no facility inspection, and no way to recall the product if something is wrong with it. If the vial is mislabeled, contaminated, or under-potent, there is nobody whose license is at stake.

A 503A compounding pharmacy is the other thing. The doctor writes the prescription. A licensed pharmacist, whose name is on the label, prepares the medicine in a facility the state inspects. If something goes wrong, there is a person and a license on the hook, and a documented chain of custody on every lot. That accountability is what makes it safe.

What is Methylene Blue?

Methylene blue is methylthioninium chloride, a synthetic phenothiazine-derived thiazine dye with the molecular formula C16H18ClN3S and a molecular weight of about 319.85 g/mol (CAS 61-73-4, PubChem

CID 6099) [3]. It was first synthesized in 1876 as a textile dye and was soon adopted in biology as a stain. It holds a place in the history of medicine as one of the earliest fully synthetic drugs, used as an antimalarial before the modern synthetic antimalarials displaced it [1210].

Its defining property is redox activity: methylene blue cycles between an oxidized blue form and a reduced colorless form (leucomethylene blue), shuttling electrons. That single chemical behavior underlies its clinical roles, from reversing methemoglobinemia to acting as an alternative mitochondrial electron carrier, and it explains why dose direction matters so much [5114].

Pharmaceutical methylene blue is a defined, USP-grade substance with controlled identity, purity, and heavy-metal limits. The same name appears on aquarium treatments and laboratory stains, but those are not pharmaceutical grade and are not medicine. The distinction is central to safe compounding [28].

How Methylene Blue Works

Methylene blue works by moving electrons. In red blood cells it is reduced to leucomethylene blue by the NADPH-dependent methemoglobin reductase system, and the reduced form then donates electrons to ferric methemoglobin (Fe3+), converting it back to functional ferrous hemoglobin (Fe2+) that can carry oxygen again. This is the mechanism behind its use as a methemoglobinemia antidote [1110].

The same molecule has two other clinically important actions. It is a potent inhibitor of monoamine oxidase A, the enzyme that breaks down serotonin, which is why combining methylene blue with serotonergic medicines can drive serotonin to toxic levels [7]. And it inhibits the nitric oxide and soluble guanylate cyclase signaling pathway that relaxes blood vessels, which is why it can raise blood pressure in vasoplegia, a state of pathological vasodilation [1314].

The dose-response is biphasic, sometimes described as hormetic. Low doses reduce methemoglobin and support mitochondrial electron transport; high doses tip the balance the other way and can cause methemoglobinemia and hemolysis. A dose calibrated for one purpose can be harmful for another, which is the core reason methylene blue rewards careful, individualized dosing [116].

Biological Role of Methylene Blue

Methylene blue is not an endogenous substance. It is a synthetic redox agent that engages endogenous systems: the erythrocyte methemoglobin-reduction machinery, monoamine oxidase A, the nitric oxide and cyclic GMP vascular signaling pathway, and the mitochondrial electron transport chain [5].

Because its effects depend on the patient's own NADPH-generating capacity, methylene blue's antidotal action is conditional on intact G6PD activity. In G6PD deficiency the supporting biochemistry is missing, so the drug is both ineffective for methemoglobinemia and dangerous, a clean example of how a fixed dose interacts with individual biology [111].

Detailed Mechanism of Methylene Blue

In the erythrocyte, the physiologic defense against methemoglobin is the cytochrome b5 reductase (NADH-dependent) system. Methylene blue opens a second, faster route: NADPH-methemoglobin reductase (NADPH diaphorase) reduces methylene blue to leucomethylene blue using NADPH generated by the hexose monophosphate shunt, and leucomethylene blue non-enzymatically reduces ferric methemoglobin to functional hemoglobin. This NADPH dependence is exactly why methylene blue fails in glucose-6-phosphate dehydrogenase (G6PD) deficiency: without adequate NADPH supply, the reduction cycle cannot run, and the unreduced dye instead acts as an oxidant that precipitates hemolysis [11101].

Monoamine oxidase A inhibition is potent and was confirmed pharmacologically by Ramsay and colleagues, who measured methylene blue as a high-affinity reversible MAO-A inhibitor, validating the earlier theoretical prediction that this enzyme inhibition is the mechanistic basis for methylene-blue-precipitated serotonin toxicity [7]. Gillman framed central-nervous-system toxicity with methylene blue as the clearest worked example of how a drug interaction precipitates serotonin syndrome, and Zuschlag and colleagues catalogued the case literature including methylene blue used as a urinary analgesic [89].

The vascular action is inhibition of the nitric oxide pathway. Mayer and colleagues showed methylene blue inhibits nitric oxide synthesis, and Evora clarified that its dominant relevant effect in vasoplegia is inhibition of soluble guanylate cyclase, the downstream enzyme that converts the vasodilatory nitric oxide signal into cyclic GMP, rather than blocking nitric oxide production itself [1314]. Inhibiting that pathway reduces excessive vasodilation, the rationale for using methylene blue in refractory vasoplegic syndrome and related distributive-shock states. The cobalamin literature describes a parallel nitric-oxide-scavenging strategy for the same physiology [27].

Beyond hemoglobin, methylene blue can act as an alternative electron carrier in the mitochondrial electron transport chain, accepting electrons and bypassing complex inhibition, which is the basis for its investigation in neurodegeneration and for the broad redox effects reviewed by Oz and colleagues [56]. The same redox versatility is double-edged: at high concentrations the oxidized dye becomes a hemoglobin oxidant, which is why escalating the dose to treat refractory methemoglobinemia can worsen it [11].

Methylene Blue Research History

Methylene blue was synthesized by Heinrich Caro in 1876 and entered medicine within two decades. Paul Ehrlich used it as a vital stain and explored it therapeutically, and it became one of the first synthetic antimalarials, a role later revisited in the modern combination-therapy era as Schirmer and colleagues summarized [12]. Its place as an antidote for methemoglobinemia was established through the twentieth century and remains its central clinical identity [1011].

The vascular pharmacology was worked out in the early 1990s. Mayer and colleagues characterized methylene blue's inhibition of nitric oxide synthesis, and the recognition that it inhibits soluble guanylate cyclase reframed the vasoplegia rationale; Evora later clarified that guanylate cyclase inhibition, not blockade of nitric oxide production, is the operative effect [13][14]. Levin and colleagues then published a randomized trial showing methylene blue reduced mortality and morbidity in vasoplegic patients after cardiac surgery, and the comparative evidence against hydroxocobalamin was synthesized by Cadd and colleagues, with supporting case series and reviews from Roderique, Burnes, Shapeton, Datt, and Denny [18][21][22][23][24][25][26].

The serotonin-toxicity story matured in parallel. Ramsay and colleagues confirmed potent monoamine oxidase A inhibition in 2007, Gillman used methylene blue as the exemplar for predicting serotonin-syndrome drug interactions, and the FDA issued Drug Safety Communications in 2011 after perioperative cases, mostly during parathyroid surgery, in patients taking serotonergic antidepressants. Zuschlag and colleagues reviewed the case literature systematically [7][8][29].

Other lines of research include ifosfamide-induced encephalopathy, where Pelgrims and colleagues reviewed treatment and prevention with methylene blue [16]; septic shock, where Kirov and colleagues ran a pilot randomized controlled study of a methylene blue infusion [17]; pharmacokinetics, where Walter-Sack and colleagues measured high absolute oral bioavailability of an aqueous formulation [15]; and neurodegeneration, where Oz and colleagues reviewed the broad cellular and molecular actions in the nervous system [5][6]. ProvayBlue earned the first modern FDA approval for acquired methemoglobinemia in 2016 [1].

Methylene Blue Timeline

- **1876** • Methylene blue synthesized by Heinrich Caro as a textile dye; soon adopted as a biological stain.
- **1891** • Used as one of the first fully synthetic antimalarial drugs; a role later revisited in the modern combination-therapy era [12]
- **1992** • van der Pol and colleagues report jejunal atresia after intra-amniotic methylene blue in genetic amniocentesis of twins, anchoring the pregnancy-harm caution [20]
- **1993** • Mayer and colleagues characterize inhibition of nitric oxide synthesis by methylene blue, foundational vascular pharmacology [13]
- **2000** • Pelgrims and colleagues review methylene blue in the treatment and prevention of ifosfamide-induced encephalopathy across 12 cases plus the prior literature [16]
- **2001** • Kirov and colleagues publish a pilot randomized controlled study of a methylene blue infusion in human septic shock [17]

2003 • Clifton and Leikin publish a clinical review of methylene blue; Schirmer and colleagues review its antimalarial role [1012]

2004 • Levin and colleagues report a randomized trial showing methylene blue reduced mortality and morbidity in vasoplegic patients after cardiac surgery [18]

2007 • Ramsay and colleagues confirm potent monoamine oxidase A inhibition by methylene blue, validating the serotonin-toxicity prediction [7]

2009 • Walter-Sack and colleagues report high absolute oral bioavailability of an aqueous methylene blue formulation; Oz and colleagues review methylene blue and Alzheimer disease [156]

2010 • Ginimuge and Jyothi publish the widely cited Methylene blue: revisited review of clinical uses and dangers [11]

2011 • Oz and colleagues review cellular and molecular actions in the nervous system; Gillman frames methylene blue as the exemplar for serotonin-toxicity interactions; the FDA issues Drug Safety Communications on the serotonergic-drug interaction [582]

2016 • FDA approves ProvayBlue (methylene blue injection, USP) for acquired methemoglobinemia in adults and pediatric patients [1]

2024 • Cadd and colleagues publish a systematic review and meta-analysis comparing hydroxocobalamin and methylene blue for vasoplegic shock following cardiopulmonary bypass [21]

Clinical Contexts for Methylene Blue

Acquired methemoglobinemia FDA APPROVED

FDA-approved indication for ProvayBlue (methylene blue injection, USP).

Acquired methemoglobinemia, caused by oxidant exposures such as topical anesthetics, dapsone, and nitrites, locks hemoglobin iron in the ferric state so it cannot carry oxygen. Methylene blue is the first-line antidote, dosed 1 mg/kg intravenously over 5 to 30 minutes with a possible repeat dose, and works through the NADPH-dependent reduction pathway. It is ineffective and contraindicated in G6PD deficiency, where the supporting NADPH supply is inadequate. [111]

Branded product: ProvayBlue (methylene blue injection, USP)

Refractory vasoplegic syndrome after cardiopulmonary bypass WELL STUDIED

Studied in a randomized trial and multiple series; off-label use with reasonable supportive evidence.

Vasoplegic syndrome is pathological vasodilation and low blood pressure that resists standard vasopressors, often after cardiopulmonary bypass. Levin and colleagues randomized vasoplegic cardiac-surgery patients and reported reduced mortality and morbidity with methylene blue, which inhibits the nitric oxide and guanylate cyclase pathway driving the vasodilation. Cadd and colleagues synthesized the comparative evidence against hydroxocobalamin, and Roderique, Burnes, Shapeton, and Datt describe the broader rescue experience. [18211422232425]

Ifosfamide-induced encephalopathy WELL STUDIED

Studied in case series and reviews; off-label use with supportive but limited evidence.

The chemotherapy agent ifosfamide can cause acute confusion and encephalopathy. Pelgrims and colleagues reviewed methylene blue used both to treat established ifosfamide encephalopathy and to prevent it in at-risk patients, reporting clinical improvement across 12 cases and the prior literature, with a proposed mechanism involving restoration of mitochondrial electron transport. [165]

Refractory septic shock EMERGING

Studied in a pilot randomized trial and small studies; remains exploratory off-label use.

Septic shock that resists vasopressors shares the same excessive nitric-oxide-driven vasodilation. Kirov and colleagues ran a pilot randomized controlled study of a continuous methylene blue infusion in human septic shock and reported improved hemodynamics and reduced vasopressor requirement, though the evidence base remains small and methylene blue is not an established standard for this indication. [1713]

Surgical tissue and fistula marking EMERGING

Long-standing intraoperative use as a visible dye; supportive and historical rather than trial-based.

Surgeons use sterile methylene blue as a visible marker to identify tissue planes, sentinel structures, fistula tracts, and leaks because of its deep color and tissue uptake. This is a dye application rather than a pharmacologic one, but the same serotonin-toxicity caution applies when intravenous or absorbed doses are given to patients on serotonergic drugs. [118]

Cyanide and historical antimalarial use EMERGING

Historical context only; superseded by modern agents.

Methylene blue has historical roles as an early synthetic antimalarial and, in older practice, as part of cyanide management, but both have been superseded by more effective and better-tolerated agents and are presented here as history rather than current recommendation. [1210]

Off-Label Uses of Methylene Blue

Refractory vasoplegia and distributive shock WELL STUDIED

Off-label rescue use with randomized and observational support in the cardiac-surgery setting.

Used as a vasopressor-sparing rescue in vasoplegic syndrome resistant to standard therapy, on the basis of Levin's randomized trial and a body of series and reviews. [182124]

Ifosfamide-induced encephalopathy WELL STUDIED

Off-label, supported by case series and reviews.

Used to treat or prevent ifosfamide encephalopathy in oncology practice, supported by the Pelgrims review. [16]

Refractory septic shock EMERGING

Off-label, exploratory; evidence is preliminary.

Explored as an adjunct in vasopressor-refractory septic shock on the basis of a pilot randomized study and small case experience. [17]

FDA-Approved Uses of Methylene Blue

Brand	Indication	Year	Route
ProvayBlue (methylene blue injection, USP)	Acquired methemoglobinemia in adult and pediatric patients	2016	Intravenous injection (5 mg/mL solution; 10 mg per 2 mL and 50 mg per 10 mL single-dose ampules or vials)
Methylene blue injection, USP (generic)	Acquired methemoglobinemia; long-marketed parenteral methylene blue used in hospital practice	—	Intravenous injection

ProvayBlue (methylene blue injection, USP) was FDA-approved in 2016 for the treatment of acquired methemoglobinemia in adult and pediatric patients. The labeled dose is 1 mg/kg given intravenously over 5 to 30 minutes, with a repeat dose of up to 1 mg/kg one hour later if the methemoglobin level stays above 30 percent or symptoms persist [1].

The label carries a prominent warning that methylene blue may cause serious or fatal serotonin toxicity when used with serotonergic drugs and opioids, and it is contraindicated in glucose-6-phosphate dehydrogenase (G6PD) deficiency because of the risk of severe hemolytic anemia and because the drug is

ineffective for methemoglobinemia in that population. The label also notes transient pulse-oximetry interference and pregnancy risk [1].

Long-marketed generic methylene blue injection USP remains in hospital use for the same antidotal purpose. Outside methemoglobinemia, the hospital uses described elsewhere on this page are off-label and rest on study-level evidence rather than FDA approval.

Compounded Methylene Blue (503A)

RonanRx compounds methylene blue under 503A on a patient-specific prescription written by a licensed prescriber for an identified patient. Two preparation pathways are relevant: a sterile intravenous preparation, prepared to USP sterile-compounding standards, when the manufactured product is not appropriate or available; and a custom low-dose oral form (capsule or solution) when a prescriber documents a clinical need that no manufactured product meets [28][30].

CHEMISTRY

MOLECULAR FORMULA
$C_{16}H_{18}ClN_3S$

MOLECULAR WEIGHT
319.85 g/mol

CAS NUMBER
61-73-4

TERMINAL HALF-LIFE
~5 to 6.5 h (oral)

Compounded use is appropriate when there is a documented patient-specific reason, for example a strength or concentration that is not manufactured, an oral route for a clinical situation where the prescriber wants low-dose oral dosing rather than an injection, or an excipient or preservative consideration for a specific patient. Because the manufactured methylene blue injection is FDA-approved, a compounded preparation is not used as a routine substitute for it; the patient-specific clinical reason is documented, consistent with FDA guidance on compounded copies of approved products [1][11][29].

The single most important compounding control is ingredient grade. Compounded methylene blue must be prepared from pharmaceutical (USP) grade methylthioninium chloride with documented identity, purity, and heavy-metal limits. Industrial dye, aquarium treatments, and internet research-chemical methylene blue are not medicine and are not used [28].

Methylene Blue Formulations and Routes

Form	Concentration	Description
Sterile injection (compounded, USP)	Custom, prepared to the prescribed strength (manufactured reference is 5 mg/mL)	Preservative-considered sterile solution prepared to USP sterile-compounding standards for intravenous administration when the manufactured methylene blue injection is not appropriate or available. Pharmaceutical-grade ingredient and sterility control are mandatory. [30]

Form	Concentration	Description
Oral capsule (compounded, low-dose)	Custom low-dose strengths set by the prescriber	Custom-strength oral capsules for clinical situations where a prescriber documents a need for low-dose oral methylene blue. Oral methylene blue has high absolute bioavailability in aqueous formulation, so dosing is conservative and prescriber-directed. [15]
Oral solution (compounded, low-dose)	Custom low-dose concentration	Custom-strength oral solution as an alternative to capsules when a measured liquid dose is preferred, prepared from pharmaceutical-grade ingredient under nonsterile compounding standards. [31]

Routes used in published literature: intravenous, oral.

Methylene Blue Dosing

Route	Population	Range	Duration	Study type
Intravenous	Adults and pediatric patients with acquired methemoglobinemia (FDA-label population)	1 mg/kg over 5 to 30 minutes; may repeat up to 1 mg/kg once after 1 hour if methemoglobin stays above 30 percent or symptoms persist	Acute antidotal dosing	FDA-approved labeled regimen (ProvayBlue)
Intravenous	Adults with refractory vasoplegic syndrome after cardiac surgery (off-label)	Commonly studied as a bolus of about 1.5 to 2 mg/kg, with or without a subsequent infusion, under specialist direction	Acute, as directed	Randomized trial and series; off-label hospital use
Intravenous	Adults with refractory septic shock (exploratory off-label)	Studied as a bolus followed by a continuous infusion in a pilot trial; not an established standard regimen	Acute, study-defined	Pilot randomized controlled study
Oral	Patients for whom a prescriber documents a low-dose oral indication	Custom low-dose, set by the prescribing clinician; oral methylene blue has high absolute bioavailability	As directed	Compounded preparation under 503A; prescriber-directed dosing

Doctor-prescribed and individualized. The FDA-labeled methemoglobinemia dose is 1 mg/kg intravenously over 5 to 30 minutes with a possible repeat dose; exceeding the cumulative dose range can paradoxically worsen methemoglobinemia and provoke hemolysis, so dose ceilings matter [1][11].

Vasoplegia and septic-shock dosing are off-label, specialist-directed, and typically given in critical-care settings under hemodynamic monitoring [1][8][17]. Before any methylene blue dose, the prescriber must screen for serotonergic medications and for G6PD deficiency, because both change the risk calculus fundamentally [17].

Compounded oral methylene blue is a low-dose preparation; its strength is selected by the prescriber and is not derived from the injectable antidote dose. Oral bioavailability is high, so conservative dosing is appropriate [15].

Methylene Blue Safety

The headline safety issue is serotonin toxicity. Methylene blue is a potent monoamine oxidase A inhibitor, and combining it with serotonergic drugs, including selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, monoamine oxidase inhibitors, and certain opioids, can cause serious or fatal serotonin syndrome. This is the subject of a 2011 FDA Drug Safety Communication and a prominent label warning, and was confirmed pharmacologically by Ramsay and framed clinically by Gillman [1][2][7][8]. Whenever feasible, serotonergic agents are held or a washout is observed before elective methylene blue exposure, and patients are monitored for serotonin-syndrome features afterward [9].

The second major issue is glucose-6-phosphate dehydrogenase (G6PD) deficiency. In this inherited condition methylene blue can cause severe hemolytic anemia and is also ineffective for methemoglobinemia because the reduction pathway it relies on cannot run. G6PD status should be considered before use, and the drug is contraindicated in known deficiency [1][11].

Methylene blue transiently interferes with pulse oximetry, producing a falsely low oxygen-saturation reading for several minutes after dosing because the dye absorbs light at the wavelengths the oximeter uses [19]. It also turns urine and stool blue-green, a benign and expected effect. In pregnancy, intra-amniotic methylene blue has been linked to fetal intestinal atresia and fetal death, so its use in pregnancy is approached with caution and reserved for situations where the benefit justifies the risk [20][1]. The dose-dependent reversal of its own benefit, helpful at low dose, harmful at high dose, is itself a safety consideration that argues for careful dosing [11].

Contraindications

Absolute and near-absolute contraindications: glucose-6-phosphate dehydrogenase (G6PD) deficiency (risk of severe hemolysis and lack of efficacy for methemoglobinemia); concurrent use of serotonergic drugs and opioids where the combination risk is not justified by an urgent indication (risk of serious or fatal serotonin toxicity); and known severe hypersensitivity to methylene blue [17].

Cautions: pregnancy, given the association of intra-amniotic exposure with fetal harm; renal impairment, because methylene blue and its metabolites are renally eliminated; and any clinical setting where escalating the dose to chase a refractory methemoglobinemia could tip the redox balance toward worsening it [12011].

Practical pre-dose checks: confirm the indication, screen the medication list for serotonergic agents, and consider G6PD status, especially in patients of African, Mediterranean, or Southeast Asian ancestry where deficiency is more common [8].

Drug interactions

Serotonergic drugs are the critical interaction. Because methylene blue potently inhibits monoamine oxidase A, co-administration with selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, monoamine oxidase inhibitors, tricyclic antidepressants, certain opioids such as meperidine and tramadol, and other serotonergic agents can precipitate serious or fatal serotonin syndrome. The FDA issued Drug Safety Communications on this interaction in 2011 after perioperative cases, and the label warns against concomitant use [217]. When methylene blue is needed for an urgent indication in a patient on serotonergic therapy, the decision is individualized and the patient is monitored closely for serotonin-syndrome features [89].

Pharmacodynamic interactions also include additive effects with other agents acting on the nitric oxide and guanylate cyclase pathway; methylene blue inhibits soluble guanylate cyclase, so its vascular effect can interact with nitric-oxide donors and related vasoactive drugs [1413].

Methylene blue interferes with co-oximetry and pulse-oximetry measurements for a period after dosing, which is a measurement interaction rather than a pharmacologic one but matters at the bedside because it can mislead oxygenation assessment [19].

Adverse events

Common and expected effects: blue-green discoloration of urine and stool, a transient blue tinge to the skin, and a metallic taste. These are benign and resolve as the drug clears [11]. Local irritation can occur at the injection site, and rapid or high-dose intravenous administration can cause nausea, abdominal pain, dizziness, sweating, and a transient rise or fall in blood pressure.

Pulse-oximetry interference: methylene blue produces a transient, artifactual fall in the pulse-oximeter oxygen-saturation reading for several minutes after dosing because the dye absorbs light at oximeter wavelengths. This is a measurement artifact, not true desaturation, and must be recognized to avoid unnecessary intervention [19].

Serious adverse events: serotonin toxicity when combined with serotonergic drugs, which can be severe or fatal and presents with agitation, autonomic instability, neuromuscular hyperactivity, and in severe cases seizures or coma [189]. Hemolytic anemia and methemoglobinemia, particularly at high doses or in G6PD deficiency, where the redox effect reverses [111]. In pregnancy, intra-amniotic exposure has caused fetal intestinal atresia and fetal death [20].

Monitoring Methylene Blue Therapy

For methemoglobinemia, treatment response is followed by repeat methemoglobin measurement (co-oximetry), recognizing that methylene blue itself transiently interferes with both pulse oximetry and co-oximetry readings; clinical status and arterial measurements are interpreted with that artifact in mind [191].

After any methylene blue dose, patients who are or may be taking serotonergic drugs are monitored for serotonin-syndrome features (agitation, tremor, hyperreflexia, autonomic instability, hyperthermia) for the period during which the interaction can manifest [81].

In patients at risk for hemolysis, hemoglobin and signs of hemolysis are followed, and the cumulative dose is kept within the safe range to avoid tipping the redox balance toward worsening methemoglobinemia [11].

Methylene Blue in Special Populations

Methylene Blue Evidence Quality

The strongest evidence supports the FDA-approved indication: acquired methemoglobinemia, where methylene blue is the established first-line antidote and ProvayBlue carries a modern FDA approval [11011]. The mechanism is well characterized, and the failure mode in G6PD deficiency is well understood [711].

For refractory vasoplegic syndrome after cardiac surgery the evidence is moderate and improving: a randomized trial by Levin, a meta-analysis by Cadd comparing methylene blue with hydroxocobalamin, and a consistent body of series and reviews from Roderique, Burnes, Shapeton, Datt, and Denny support its use as a vasopressor-sparing rescue, with the mechanism clarified by Mayer and Evora [182122232425261314].

For ifosfamide-induced encephalopathy the evidence is case-series and review level (Pelgrims), and for septic shock it is pilot-trial level (Kirov); both are off-label and neither is an established standard [1617]. The neuroscience literature reviewed by Oz documents broad redox and mitochondrial actions that remain investigational [56]. Across indications, the serotonin-toxicity and G6PD-deficiency facts are settled and govern safe use [289].

Major Methylene Blue Clinical Studies

Study	Design	Participants	Duration	Finding
Levin 2004 (Ann Thorac Surg), Methylene blue in	Randomized controlled trial	100	Perioperative	**In a randomized study, giving methylene blue to**

Study	Design	Participants	Duration	Finding
vasoplegic patients after cardiac surgery				**heart-surgery patients whose blood pressure stayed dangerously low led to fewer deaths and complications.** *Methylene blue reduced mortality and morbidity versus standard care in patients with vasoplegic syndrome after cardiac surgery, supporting its use as a rescue for refractory vasodilation.* [18]
Cadd 2024 (J Cardiothorac Vasc Anesth), Hydroxocobalamin versus methylene blue for vasoplegic shock	Systematic review and meta-analysis	—	Cumulative	**A review that pooled prior studies compared methylene blue with another rescue drug for dangerously low blood pressure after heart-lung-bypass surgery.** *Pooled the comparative evidence for hydroxocobalamin and methylene blue in vasoplegic shock following cardiopulmonary bypass, informing agent selection in refractory vasoplegia.* [21]
Kirov 2001 (Crit Care Med), Methylene blue infusion in human septic shock	Pilot randomized controlled study	20	Acute	**In a small pilot study, a steady drip of methylene blue helped raise blood pressure and reduced the need for other blood-pressure drugs in patients with severe infection.** *A continuous methylene blue infusion improved hemodynamics and reduced vasopressor requirement in septic shock; the trial was small and exploratory.* [17]
Pelgrims 2000 (Br J Cancer), Methylene blue for ifosfamide-induced encephalopathy	Case series and literature review	12	Acute	**Methylene blue helped reverse and prevent the confusion that the chemotherapy drug**

Study	Design	Participants	Duration	Finding
				ifosfamide can cause, across a series of patients. *Methylene blue was used to treat and to prevent ifosfamide-induced encephalopathy with clinical improvement across 12 cases and the prior literature.* [16]
Ramsay 2007 (Br J Pharmacol), Methylene blue and serotonin toxicity	Pharmacological enzyme-inhibition study	—	In vitro	**Lab work confirmed that methylene blue strongly blocks the enzyme that breaks down serotonin, which is why mixing it with certain antidepressants is dangerous.** *Confirmed that methylene blue is a potent inhibitor of monoamine oxidase A, validating the prediction that this enzyme inhibition underlies methylene-blue-precipitated serotonin toxicity.* [7]
Walter-Sack 2009 (Eur J Clin Pharmacol), Oral bioavailability of methylene blue	Pharmacokinetic study	—	Single dose	**When taken by mouth as a water-based solution, methylene blue was absorbed well into the bloodstream.** *An aqueous oral methylene blue formulation showed high absolute bioavailability, characterizing the oral route relevant to compounded low-dose oral preparations.* [15]
Mayer 1993 (Biochem Pharmacol), Inhibition of nitric oxide synthesis by methylene blue	Biochemical mechanism study	—	In vitro	**Lab work showed how methylene blue interferes with the body signal that relaxes blood vessels, which explains why it can raise blood pressure.** *Characterized methylene blue's inhibition of the nitric oxide pathway, foundational to its*

Study	Design	Participants	Duration	Finding
				vascular and vasoplegia pharmacology. [13]
Zuschlag 2018 (Psychosomatics), Methylene blue-induced serotonin syndrome review	Case report and systematic literature review	—	Cumulative	**A review of reported cases confirmed that methylene blue can trigger serotonin syndrome in people taking serotonin-affecting medicines.** *Systematically reviewed reported cases of methylene-blue-induced serotonin syndrome, including exposures via urinary analgesics, reinforcing the interaction warning.* [9]

Methylene Blue Pharmacokinetics & Pharmacodynamics

Pharmacokinetics

Given intravenously, methylene blue distributes rapidly into tissues, is reduced to leucomethylene blue, and is eliminated in urine and bile, with a portion of the dose excreted as the colorless reduced form and a portion as the blue oxidized form, which accounts for the characteristic blue-green discoloration of urine [11]. The drug and its metabolites undergo renal elimination, so renal function influences clearance [1].

Oral methylene blue is well absorbed: Walter-Sack and colleagues measured high absolute bioavailability for an aqueous oral formulation, which is the pharmacokinetic basis for using a conservative, prescriber-set low dose in compounded oral preparations [15]. Onset for the antidotal effect in methemoglobinemia is rapid after intravenous dosing, with clinical improvement typically within minutes to an hour [1].

Pharmacodynamics

Pharmacodynamically, methylene blue's effect is direction-dependent on dose and on the patient's redox biochemistry. At low concentration it reduces methemoglobin and supports mitochondrial electron transport; at high concentration the oxidized dye becomes a hemoglobin oxidant [115].

Its inhibition of monoamine oxidase A raises synaptic serotonin and creates the serotonin-toxicity risk, and its inhibition of soluble guanylate cyclase reduces nitric-oxide-mediated vasodilation, raising vascular tone in vasoplegia [714]. These are simultaneous actions of one molecule, which is why indication and dose, not the drug alone, determine the benefit-risk balance.

Comparing Methylene Blue Formulations

The manufactured reference is methylene blue injection, USP, a sterile 5 mg/mL solution used intravenously for methemoglobinemia (ProvayBlue and long-marketed generics) [1]. This is the formulation behind the FDA-approved antidotal use and the off-label hospital uses described above.

RonanRx-compounded preparations are dispensed only on a patient-specific prescription when the manufactured product is not appropriate or available, or when a prescriber documents a need for a low-dose oral form. A compounded sterile injection follows sterile-compounding standards; a compounded oral capsule or solution is a low-dose preparation whose strength is set by the prescriber and is not bioequivalent to, or scaled from, the injectable antidote dose [3015].

Methylene Blue Storage and Handling

Methylene blue solutions are stored protected from light, because light and oxidation affect the dye, and at the temperature specified for the preparation; the manufactured injection is stored at controlled room temperature per its labeling [1].

Compounded sterile injections and compounded oral preparations carry beyond-use dates set by the dispensing pharmacy from the formulation record and the applicable compounding standards; patients follow the dispensing label for storage and beyond-use date [3031].

Methylene Blue Compounding & Operations

503A compounding

RonanRx prepares methylene blue under 503A on a patient-specific prescription written by a licensed prescriber for an identified patient, consistent with section 503A of the Federal Food, Drug, and Cosmetic Act [28]. Sterile injectable preparations are made to USP sterile-compounding standards; nonsterile oral preparations are made to nonsterile-compounding standards [3031].

The defining quality control for this compound is ingredient grade. Pharmaceutical (USP) grade methylthioninium chloride is used, with a certificate of analysis documenting identity, purity, and heavy-metal limits. Industrial, aquarium, and research-chemical methylene blue is explicitly excluded. Because the dose-response is biphasic, the prescribed strength and route are verified against the documented clinical purpose so that a low-dose oral preparation is never confused with the higher injectable antidote dose [2811].

Pharmacist review

Each prescription for compounded methylene blue is reviewed by a licensed pharmacist before dispensing. The review confirms a documented patient-specific clinical reason, the appropriate route and strength for the stated purpose, and the safety screen that this molecule demands: the patient's medication list is checked for serotonergic drugs because of the serotonin-toxicity risk, and G6PD status is considered because of the hemolysis risk and lack of efficacy in deficiency [71].

The pharmacist confirms that the prescribed strength is consistent with the documented indication and within a safe range, that the ingredient is pharmaceutical (USP) grade, and that the preparation is dispensed for patient-specific 503A use rather than for direct-to-consumer or office-stock distribution [28].

Quality and traceability

Methylene blue active ingredient (USP-grade methylthioninium chloride) is sourced from FDA-registered suppliers with documented certificates of analysis. Each preparation carries a lot number tied to the prescription record, the API source, the compounding date, the beyond-use date, and the dispensing pharmacist of record. Sterile injectable preparations follow sterility and endotoxin controls per USP sterile-compounding standards, and records are retained per state board of pharmacy requirements [30].

Cold chain

Compounded methylene blue preparations are stored protected from light. Oral capsules and solutions are generally stable at controlled room temperature; sterile injectable preparations follow the storage and beyond-use conditions on the dispensing label, and patients are advised to follow that label and to contact the pharmacy if storage integrity is in doubt [30].

Frequently Asked Questions About Methylene Blue

What is methylene blue approved for?

The FDA-approved use is treating acquired methemoglobinemia, a condition in which the blood cannot carry oxygen properly. The approved injectable product is ProvayBlue, cleared in 2016 for adults and children, dosed at 1 mg/kg intravenously with a possible repeat dose [1]. Other hospital uses, such as for low blood pressure after heart surgery, are off-label and based on study evidence rather than FDA approval.

Why can't methylene blue be combined with antidepressants?

Methylene blue strongly blocks an enzyme (monoamine oxidase A) that breaks down serotonin. Combining it with antidepressants and other serotonin-affecting drugs, including SSRIs, SNRIs, MAOIs, and some opioids, can cause serotonin syndrome, which can be severe or fatal. The FDA warned about this in 2011, and it appears prominently on the drug label [217].

Who should not receive methylene blue?

People with glucose-6-phosphate dehydrogenase (G6PD) deficiency should not receive it: it can cause severe breakdown of red blood cells, and it does not work for methemoglobinemia in that condition. People taking serotonin-affecting medicines and people with a known severe allergy to methylene blue are also at risk, and it is used cautiously in pregnancy [111].

Why did my oxygen reading drop and my urine turn blue?

Both are expected. Methylene blue briefly absorbs light at the wavelengths a pulse oximeter uses, so it can make the oxygen reading look falsely low for a few minutes; this is a measurement artifact, not real low oxygen [19]. The blue-green color in urine and stool is the dye being eliminated and is harmless [11].

Is aquarium or research-chemical methylene blue the same thing?

No. Medicine uses pharmaceutical (USP) grade methylene blue with documented identity, purity, and heavy-metal limits. Aquarium treatments and internet research-chemical methylene blue are not pharmaceutical grade and are not medicine. Compounded methylene blue at RonanRx is prepared only from USP-grade ingredient on a patient-specific prescription [28].

Does RonanRx sell methylene blue directly to patients?

No. Compounded methylene blue requires a patient-specific prescription written by a licensed prescriber for an identified patient, plus pharmacist review before dispensing. RonanRx is not a direct-to-consumer storefront, and methylene blue's serotonin and G6PD safety issues make physician direction essential [287].

References

1. *[fda_label_provayblue]* Provepharm / U.S. Food and Drug Administration. *PROVAYBLUE (methylene blue) injection, USP, for intravenous use — Prescribing Information (DailyMed)*. DailyMed. 2016. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=4f6848e5-35ed-4046-b13c-3032b5ba3232 (accessed 2026-06-26)
2. *[fda_dsc_serotonin]* U.S. Food and Drug Administration. *FDA Drug Safety Communication: Serious CNS reactions possible when methylene blue is given to patients taking certain psychiatric medications*. FDA Drug Safety Communication. 2011. https://wayback.archive-it.org/7993/20170112031630/http://www.fda.gov/Drugs/DrugSafety/ucm263190.htm (accessed 2026-06-26)
3. *[pubchem_mb]* National Center for Biotechnology Information. *Methylene Blue (Methylthioninium chloride), PubChem CID 6099*. PubChem Compound Summary. 2026. https://pubchem.ncbi.nlm.nih.gov/compound/6099 (accessed 2026-06-26)
4. *[statpearls_mb]* StatPearls. *Methylene Blue*. StatPearls Publishing. 2024. https://www.ncbi.nlm.nih.gov/books/NBK557593/ (accessed 2026-06-26)
5. *[oz2011nervous]* Oz M, Lorke DE, Hasan M, Petroianu GA. *Cellular and molecular actions of Methylene Blue in the nervous system.*. Medicinal Research Reviews. 2011. PMID 19760660. (accessed 2026-06-26)

6. *[oz2009alzheimer]* Oz M, Lorke DE, Petroianu GA. *Methylene blue and Alzheimer's disease.*. Biochemical Pharmacology. 2009. PMID 19433072. (accessed 2026-06-26)
7. *[ramsay2007mao]* Ramsay RR, Dunford C, Gillman PK. *Methylene blue and serotonin toxicity: inhibition of monoamine oxidase A (MAO A) confirms a theoretical prediction.*. British Journal of Pharmacology. 2007. PMID 17721552. (accessed 2026-06-26)
8. *[gillman2011cns]* Gillman PK. *CNS toxicity involving methylene blue: the exemplar for understanding and predicting drug interactions that precipitate serotonin toxicity.*. Journal of Psychopharmacology. 2011. PMID 20142303. (accessed 2026-06-26)
9. *[zuschlag2018serotonin]* Zuschlag ZD, Warren MW, K Schultz S. *Serotonin Toxicity and Urinary Analgesics: A Case Report and Systematic Literature Review of Methylene Blue-Induced Serotonin Syndrome.*. Psychosomatics. 2018. PMID 30104021. (accessed 2026-06-26)
10. *[clifton2003mb]* Clifton J 2nd, Leikin JB. *Methylene blue.*. American Journal of Therapeutics. 2003. PMID 12845393. (accessed 2026-06-26)
11. *[ginimuge2010revisited]* Ginimuge PR, Jyothi SD. *Methylene blue: revisited.*. Journal of Anaesthesiology Clinical Pharmacology. 2010. PMID 21547182. (accessed 2026-06-26)
12. *[schirmer2003antimalarial]* Schirmer RH, Coulibaly B, Stich A, Scheiwein M, Merkle H, Eubel J, Becker K. *Methylene blue as an antimalarial agent.*. Redox Report. 2003. PMID 14962363. (accessed 2026-06-26)
13. *[mayer1993nos]* Mayer B, Brunner F, Schmidt K. *Inhibition of nitric oxide synthesis by methylene blue.*. Biochemical Pharmacology. 1993. PMID 7679577. (accessed 2026-06-26)
14. *[evora2016gc]* Evora PR. *Methylene Blue Is a Guanylate Cyclase Inhibitor That Does Not Interfere with Nitric Oxide Synthesis.*. Texas Heart Institute Journal. 2016. PMID 27047301. (accessed 2026-06-26)
15. *[walter2009bioavail]* Walter-Sack I, Rengelshausen J, Oberwittler H, Burhenne J, Mueller O, Meissner P, Mikus G. *High absolute bioavailability of methylene blue given as an aqueous oral formulation.*. European Journal of Clinical Pharmacology. 2009. PMID 18810398. (accessed 2026-06-26)
16. *[pelgrims2000ifosfamide]* Pelgrims J, De Vos F, Van den Brande J, Schrijvers D, Prové A, Vermorken JB. *Methylene blue in the treatment and prevention of ifosfamide-induced encephalopathy: report of 12 cases and a review of the literature.*. British Journal of Cancer. 2000. PMID 10646879. (accessed 2026-06-26)
17. *[kirov2001septic]* Kirov MY, Evgenov OV, Evgenov NV, Egorina EM, Sovershaev MA, Sveinbjørnsson B, Nedashkovsky EV. *Infusion of methylene blue in human septic shock: a pilot, randomized, controlled study.*. Critical Care Medicine. 2001. PMID 11588440. (accessed 2026-06-26)
18. *[levin2004vasoplegia]* Levin RL, Degrange MA, Bruno GF, Del Mazo CD, Taborda DJ, Griotti JJ, Boullon FJ. *Methylene blue reduces mortality and morbidity in vasoplegic patients after cardiac surgery.*. The Annals of Thoracic Surgery. 2004. PMID 14759425. (accessed 2026-06-26)
19. *[sidi1987oximetry]* Sidi A, Paulus DA, Rush W, Gravenstein N, Davis RF. *Methylene blue and indocyanine green artifactually lower pulse oximetry readings of oxygen saturation. Studies in dogs.*. Journal of Clinical Monitoring. 1987. PMID 3681358. (accessed 2026-06-26)
20. *[vanderpol1992atresia]* van der Pol JG, Wolf H, Boer K, Treffers PE, Leschot NJ, Hey HA. *Jejunal atresia related to the use of methylene blue in genetic amniocentesis in twins.*. British Journal of Obstetrics and Gynaecology. 1992. PMID 1554667. (accessed 2026-06-26)
21. *[cadd2024]* Cadd M, Watson U, Kilpatrick T, Hardy B, Gallop L, Gerard A, Cabaret C. *Hydroxocobalamin Versus Methylene Blue for Treatment of Vasoplegic Shock Following Cardiopulmonary Bypass: A Systematic Review and Meta-analysis*. Journal of Cardiothoracic and Vascular Anesthesia. 2024. PMID 39438181. (accessed 2026-06-26)

22. *[roderique2014]* Roderique JD, VanDyck K, Holman B, Tang D, Chui B, Spiess BD. *The use of high-dose hydroxocobalamin for vasoplegic syndrome*. Annals of Thoracic Surgery. 2014. PMID 24792267. (accessed 2026-06-26)
23. *[burnes2017]* Burnes ML, Boettcher BT, Woehlck HJ, Zundel MT, Iqbal Z, Pagel PS. *Hydroxocobalamin as a Rescue Treatment for Refractory Vasoplegic Syndrome After Prolonged Cardiopulmonary Bypass*. Journal of Cardiothoracic and Vascular Anesthesia. 2017. PMID 27838199. (accessed 2026-06-26)
24. *[shapeton2019]* Shapeton AD, Mahmood F, Ortoleva JP. *Hydroxocobalamin for the Treatment of Vasoplegia: A Review of Current Literature and Considerations for Use*. Journal of Cardiothoracic and Vascular Anesthesia. 2019. PMID 30217583. (accessed 2026-06-26)
25. *[datt2021]* Datt V, Wadhhwa R, Sharma V, Virmani S, Minhas HS, Malik S. *Vasoplegic syndrome after cardiovascular surgery: A review of pathophysiology and outcome-oriented therapeutic management*. Journal of Cardiac Surgery. 2021. PMID 34251716. (accessed 2026-06-26)
26. *[denny2015vasoplegia]* Denny JT, Burr AT, Balzer F, Tse JT, Denny JE, Chyu D. *Methylene blue treatment for cytokine release syndrome-associated vasoplegia following a renal transplant with rATG infusion: A case report and literature review.*. Experimental and Therapeutic Medicine. 2015. PMID 26136914. (accessed 2026-06-26)
27. *[weinberg2009]* Weinberg JB, Chen Y, Jiang N, Beasley BE, Salerno JC, Ghosh DK. *Inhibition of nitric oxide synthase by cobalamins and cobinamides*. Free Radical Biology and Medicine. 2009. PMID 19328848. (accessed 2026-06-26)
28. *[fda503a]* U.S. Food and Drug Administration. *Compounding Laws and Policies — Section 503A of the Federal Food, Drug, and Cosmetic Act*. FDA Drug Compounding. 2024. https://www.fda.gov/drugs/human-drug-compounding/compounding-laws-and-policies (accessed 2026-06-26)
29. *[fda_essentially_a_copy]* U.S. Food and Drug Administration. *Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act — Guidance for Industry*. FDA Guidance for Industry. 2018. https://www.fda.gov/media/98973/download (accessed 2026-06-26)
30. *[usp_797]* United States Pharmacopeia. *USP General Chapter <797> Pharmaceutical Compounding — Sterile Preparations*. USP Compounding Compendium. 2023. https://www.usp.org/compounding/general-chapter-797 (accessed 2026-06-26)
31. *[usp_795]* United States Pharmacopeia. *USP General Chapter <795> Pharmaceutical Compounding — Nonsterile Preparations*. USP Compounding Compendium. 2023. https://www.usp.org/compounding/general-chapter-795 (accessed 2026-06-26)

How to Access Methylene Blue

Compounded Methylene Blue is dispensed under 503A on a patient-specific prescription. Depending on your role, the next step looks different.

FOR PRESCRIBING CLINICIANS

Offer this medication

A pharmacist will follow up within two business days. We'll cover state availability, supported formulations, and what integration looks like for your clinic.

`ronanrx.com/request-partnership-call`

PATIENT WITH A DOCTOR

Receive your prescription

If your doctor has prescribed Methylene Blue, sign up so we can prepare and ship your medication. The signup wizard collects intake and connects you to the prescribing workflow.

`ronanrx.com/patients`

PATIENT WITHOUT A DOCTOR

Find a partner clinic

RonanRx prescribes through partner clinics — we don't initiate prescriptions on this site. Read how the referral process works and how to find a partner clinic in your state.

`ronanrx.com/find-clinic`

Other compounds RonanRx makes

This monograph is one of many in the RonanRx formulary. Every compound below is prepared under 503A on a patient-specific prescription. Browse the full catalog at ronanrx.com/medications and ronanrx.com/peptides, or scan the codes at right for each index.

Medications

Peptides

MEDICATIONS (42)

Alpha-Lipoic Acid (ALA) — Antioxidant & mitochondrial
Coenzyme Q10 (CoQ10) — Antioxidant & mitochondrial
Glutathione — Antioxidant & mitochondrial
Methylene Blue — Antioxidant & mitochondrial
NAD+ / NMN — Antioxidant & mitochondrial
Compounded Topical Anesthetics (BLT, LET) — Dermatology
Topical Minoxidil — Dermatology
Topical Tretinoin — Dermatology
Compounded Magnesium — Energy & nutritional
Cyanocobalamin — Energy & nutritional
High-Dose Vitamin D — Energy & nutritional
Hydroxocobalamin — Energy & nutritional
Iron (Compounded) — Energy & nutritional
L-Carnitine — Energy & nutritional
Methylcobalamin (B12) — Energy & nutritional
Methylfolate — Energy & nutritional
Anastrozole — Hormone optimization
Clomiphene & Enclomiphene — Hormone optimization
DHEA — Hormone optimization
Estradiol — Hormone optimization
Estriol — Hormone optimization
Human Chorionic Gonadotropin (HCG) — Hormone optimization
Oxytocin — Hormone optimization
Pregnenolone — Hormone optimization
Progesterone — Hormone optimization
Testosterone — Hormone optimization
Compounded Metformin — Metabolic & weight
Compounded Semaglutide — Metabolic & weight
Compounded Tirzepatide — Metabolic & weight
Lipotropic Injection (MIC, MICC) — Metabolic & weight
Low-Dose Naltrexone (LDN) — Metabolic & weight
Naltrexone-Bupropion Combination — Metabolic & weight
Topiramate — Metabolic & weight
Bremelanotide / PT-141 — Sexual health
Compounded Sildenafil — Sexual health
Compounded Tadalafil — Sexual health
Trimix Injection — Sexual health
Compounded Gabapentin — Sleep & recovery
Compounded Melatonin — Sleep & recovery
Compounded T3 (Liothyronine) — Thyroid
Compounded T3/T4 Combinations — Thyroid
Compounded T4 (Levothyroxine) — Thyroid

PEPTIDES (21)

Sermorelin — Available now

Tesamorelin — Available now

AOD-9604 — Growth-hormone axis (under FDA review)

CJC-1295 — Growth-hormone axis (under FDA review)

GHRP-2 / GHRP-6 — Growth-hormone axis (under FDA review)

Hexarelin — Growth-hormone axis (under FDA review)

Ipamorelin — Growth-hormone axis (under FDA review)

MK-677 / Ibutamoren — Growth-hormone axis (under FDA review)

5-Amino 1MQ — Metabolic & longevity (under FDA review)

Epitalon / Epithalon — Metabolic & longevity (under FDA review)

MOTS-C — Metabolic & longevity (under FDA review)

Thymosin Alpha-1 / Thymalin — Metabolic & longevity (under FDA review)

DSIP, Delta Sleep-Inducing Peptide — Neuro & cognitive (under FDA review)

Selank — Neuro & cognitive (under FDA review)

Semax — Neuro & cognitive (under FDA review)

Vasoactive Intestinal Peptide (VIP) — Neuro & cognitive (under FDA review)

BPC-157 — Tissue repair (under FDA review)

KPV — Tissue repair (under FDA review)

LL-37 — Tissue repair (under FDA review)

Pentadeca Arginate (PDA) — Tissue repair (under FDA review)

TB-500 / Thymosin Beta-4 — Tissue repair (under FDA review)