

# Methylene Blue

## Newborn use only

2022

<b>Alert</b>	It should be prescribed in mg/kg ( <b>NOT mL/kg</b> ) as potential dosing error can occur between mg and mL. Methylene blue is also known as methylthionium chloride.
<b>Indication</b>	Methaemoglobinaemia
<b>Action</b>	In the red blood cell, methylene blue is reduced to leukomethylene blue. Leukomethylene blue then interacts with methaemoglobin (MetHb) to reduce the ferric iron back to ferrous iron. <sup>(1,2)</sup>
<b>Drug type</b>	Antidote for methaemoglobinaemia
<b>Trade name</b>	Methylene Blue Injection (Phebra). Proveblue (Clinect).
<b>Presentation</b>	Methylene Blue Injection contains methylene blue trihydrate 50 mg/5 mL (10 mg/mL) (= 1%). Proveblue contains methylene blue trihydrate 50mg/10mL (5 mg/mL) (= 0.5%).
<b>Dose</b>	<b>1 mg/kg/dose</b> Dose can be repeated after 1 hour if MetHb remains over 30% or remain symptomatic. <sup>(1, 5)</sup>
<b>Dose adjustment</b>	Therapeutic hypothermia – No information. ECMO – No Information. Renal impairment – Use with caution in severe renal impairment. Hepatic impairment – No information.
<b>Maximum dose</b>	2 mg/kg/dose (not per day)
<b>Total cumulative dose</b>	
<b>Route</b>	IV
<b>Preparation</b>	Administer undiluted. If required can be diluted with dextrose 5% only. .
<b>Administration</b>	IV infusion over 5 minutes. Line can be flushed with sodium chloride 0.9% to reduce venous irritation.
<b>Monitoring</b>	MetHb concentration at 1 hour after the dose (Neofax states to monitor MetHb during treatment and until resolution of methaemoglobinaemia). Pulse oximetry for at least 24 hours. FBC: 24 hours after the dose (earlier if concerns of haemolytic anaemia). Extravasation: Methylene blue has a pH of 3 – 4.5 and extravasation may cause tissue necrosis.
<b>Contraindications</b>	Hypersensitivity to any component of methylene blue.
<b>Precautions</b>	Severe renal insufficiency <sup>(4)</sup> G6PD deficiency <sup>(4)</sup>
<b>Drug interactions</b>	
<b>Adverse reactions</b>	Dose-related toxicity is described. <sup>(4)</sup> At 2-4 mg/kg/dose: Haemolytic anaemia, skin desquamation. At >4 mg/kg/dose: Blue-green discolouration of urine and faeces. At 7 mg/kg/dose: Nausea, vomiting, abdominal pain, fever, and haemolysis. At 20 mg/kg/dose: Hypotension. At 80 mg/kg/dose: Bluish discolouration of skin (similar to cyanosis). This can be treated topically with diluted hypochlorite solution. Methylene blue is an oxidant and itself can increase MetHb concentrations. <sup>(2)</sup> Risk of anaphylaxis.
<b>Compatibility</b>	Fluids: Glucose 5%. <sup>(5)</sup> Y-site: Not tested.
<b>Incompatibility</b>	Fluids: Sodium chloride 0.9%, sodium chloride 0.45%, all strengths of sodium chloride + glucose combination fluids. Y-site: Not tested.
<b>Stability</b>	Use immediately. Discard unused portion.

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<b>Storage</b>	Store below 25°C. Protect from light.
<b>Excipients</b>	Methylene Blue Injection: Water for injections, sodium hydroxide and/or hydrochloric acid. <sup>(3)</sup> Proveblue: Water for injections.
<b>Special comments</b>	Methylene Blue Injection should not be diluted with sodium chloride 0.9% as precipitation may occur (due to presence of chloride ions which have been shown to reduce the solubility of methylene blue). <sup>(3)</sup>
<b>Evidence</b>	<p><b>Background</b> Methaemoglobin (MetHb) level in the human body is usually maintained below 1.5% of total haemoglobin.<sup>(2)</sup> Symptomatic methaemoglobinaemia is usually observed when MetHb concentrations exceed 15%.<sup>(1)</sup></p> <p><b>Efficacy</b> Treatment of choice for methaemoglobinaemia is 1 mg/kg of methylene blue infused intravenously over 5 minutes. Additional doses can be given if symptoms persist or methaemoglobin levels remain high. The suggested high MetHb concentrations varied from 30% to 60%.<sup>(1, 2, 4, 7)</sup></p> <p><b>Safety</b> Methylene blue has dose-related toxicity.<sup>(4)</sup> Even 2 mg/kg/dose can rarely cause haemolytic anaemia. Methylene blue doses over 4 mg/kg can exhibit an oxidizing effect and result in haemolysis and methaemoglobin production. Methaemoglobinaemia in these individuals is best treated with blood transfusions.<sup>(4)</sup></p> <p><b>Pharmacokinetics</b> After IV administration, time to reach peak effect is within 30 minutes. It is eliminated in bile, faeces and urine as leukomethylene blue.<sup>(4)</sup></p>
<b>Practice points</b>	
<b>References</b>	<ol style="list-style-type: none"> <li>Berant R, Ratnapalan S. A pale baby with blue blood. Pediatric Emergency Care. 2015;31(10):713-4.</li> <li>Johnson SF. Methemoglobinemia: Infants at risk. Current Problems in Pediatric and Adolescent Health Care. 2019;49(3):57-67.</li> <li>Methylene blue injection. Phebra Pty Ltd. MIMS online accessed online on 7 April 2022.</li> <li>Clifton J, 2nd, Leikin JB. Methylene blue. American Journal of Therapeutics. 2003;10(4):289-91.</li> <li>Methylene blue. Micromedex online. Accessed on 8 April 2022.</li> <li>Methylene blue. Australian injectable drugs handbook, 8th edition. Accessed online on 8 April 2022.</li> <li>Ward J, Motwani J, Baker N, Nash M, Ewer AK, Toldi G. Congenital Methemoglobinemia Identified by Pulse Oximetry Screening. Pediatrics. 2019;143(3):03.</li> </ol>

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