



## Dimercaprol

Updated: January 3, 2018.

## OVERVIEW

### Introduction

Dimercaprol, or British anti-Lewisite (BAL), is a parenterally administered heavy metal chelating agent that is used to treat arsenic, gold, copper and mercury poisoning. Dimercaprol has not been associated with serum enzyme elevations during therapy or with cases of clinically apparent liver injury with jaundice, but its general use has been quite limited.

### Background

Dimercaprol (dye" mer cap' rol) is a parenterally administered heavy metal chelating agent which has been used to treat arsenic, copper, gold, lead and mercury poisoning as well as severe cases of Wilson disease. Dimercaprol was developed at Oxford University during World War II as a means of treating and reversing poisoning from Lewisite, an arsenical gas used in chemical warfare (and thus initially called British anti-Lewisite [BAL]). Dimercaprol is a simple propanol molecule with two sulfhydryl groups that acts by binding heavy metals, and thus competing and blocking the binding of the toxic metals to sulfhydryl containing metabolic enzymes. Dimercaprol binds mercury, lead, copper, gold and arsenic, and its major current indications are for poisoning with arsenic, gold and mercury and, in combination with EDTA-calcium, acute lead poisoning. In addition, dimercaprol has been used to chelate copper in patients with Wilson disease, but now has been replaced by better tolerated oral chelating agents such as penicillamine and trientine. Dimercaprol is occasionally used in the initial treatment of severe, symptomatic Wilson disease, but generally for a short time only. Dimercaprol is available in solution in oil in ampules of 300 mg (100 mg/mL) generically and under the name BAL. The recommended dose and regimen vary by indication, but are in the range of 2.5 to 5 mg/kg two to five times daily, given by deep intramuscular injection for 2 to 10 days. Dimercaprol is not indicated and may be harmful in iron, cadmium and selenium poisoning. Side effects include injection site reactions, local pain and sterile abscesses as well as systemic symptoms such as nausea, vomiting, headache, dizziness, spasms, sweating, excessive lacrimation or salivation, and skin or body tingling, burning and pain. Rare, but potentially severe adverse events include seizures, stupor and coma.

### Hepatotoxicity

In clinical trials conducted in children with Wilson disease, serum aminotransferase levels generally improved or were stable during treatment with dimercaprol. There have been no clinical reports of acute liver injury with jaundice attributed to dimercaprol. Patients with Wilson disease typically have mild-to-moderate serum aminotransferase elevations and may have signs and symptoms of cirrhosis. Improvement in liver injury in Wilson disease typically requires months to years of treatment. The apparent lack of hepatotoxicity of

dimercaprol may be due to the infrequency of its use, the typically short courses of therapy and the prominence of other side effects that limit its more prolonged administration.

Likelihood score: E (unlikely cause of clinically apparent liver injury).

Drug Class: [Chelating Agents](#), [Wilson Disease Agents](#)

Other Drugs in the Subclass, Wilson Disease: [Penicillamine](#), [Trientine](#), [Zinc](#)

## PRODUCT INFORMATION

### REPRESENTATIVE TRADE NAMES

Dimercaprol – Generic, BAL®

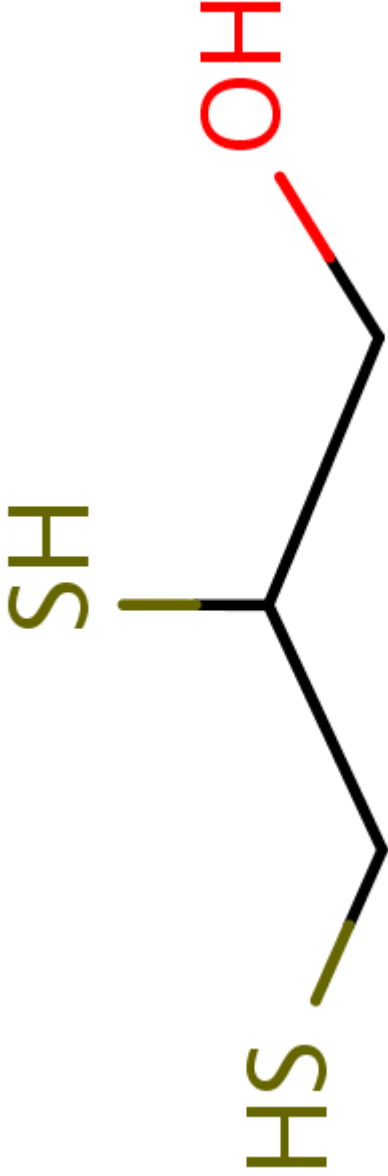
### DRUG CLASS

Chelating Agents

### COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

## CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NO.	MOLECULAR FORMULA	STRUCTURE
Dimercaprol	59-52-9	C <sub>3</sub> H <sub>8</sub> O-S <sub>2</sub>	 <p>The chemical structure of Dimercaprol is a six-membered ring consisting of five carbon atoms and one sulfur atom. The sulfur atom is located at the top vertex of the ring and is bonded to a hydrogen atom (H) and a hydroxyl group (OH). The hydroxyl group is shown in red, with the oxygen atom (O) and hydrogen atom (H) both in red. The sulfur atom and its associated bonds are shown in green. The remaining four carbon atoms form a pentagon, with each carbon atom bonded to two hydrogen atoms (H) and one sulfur atom (S). The C-S bonds are shown in green, and the C-H bonds are shown in black. The hydrogen atoms are shown in black.</p>

## ANNOTATED BIBLIOGRAPHY

References updated: 03 January 2018

Zimmerman HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999.

*(Review of hepatotoxicity published in 1999; dimercaprol is not discussed).*

Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier, 2013.

*(Textbook on hepatotoxicity; chelating agents are not discussed).*

Byrns MC, Penning TM. Treatment of metal exposure. Environmental toxicology: carcinogens and heavy metals. In, Brunton LL, Chabner BA, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 12th ed. New York: McGraw-Hill, 2011, pp. 1872-6.

*(Textbook of pharmacology and therapeutics).*

Denny-Brown D, Porter H. The effect of BAL(2,3-dimercaptopropanol) on hepatolenticular degeneration(Wilson's disease). N Engl J Med 1951; 245: 917-25. PubMed PMID: 14882450.

*(Studies of 5 patients with Wilson disease and neurologic complications treated with multiple 24 hour courses of intramuscular BAL found marked improvement in tremor and rigidity and increase in cupruresis).*

Dimercaprol for hepatolenticular degeneration. Lancet 1952; 1 (6700): 199-200. PubMed PMID: 14889814.

*(Initially used as an antidote for wartime arsenical gas poisoning, BAL was then found to increase excretion of other metals, and later shown to improve symptoms of Wilson disease, to increase urinary excretion of copper 2 to 7 times, and to not worsen liver disease).*

Warnock CG, Neill DW. Dimercaprol in the pre-neurological stage of Wilson's disease(hepatolenticular degeneration). J Neurol Neurosurg Psychiatry 1954; 17: 70-4. PubMed PMID: 13131080.

*(Treatment of a 12 year old child with Wilson disease [of which two siblings had died], without neurologic symptoms, with multiple courses of BAL showed marked increase in copper excretion and improvement in liver disease).*

Bearn AG. The place of BAL in the therapy of Wilson's disease. Am J Med 1956; 21: 134. Not in PubMed

*(Among patients with Wilson disease treated with BAL in doses of 200 to 300 mg twice daily for several months, injections were often painful and toxic reactions included high fever, worsening of neurologic signs, hallucinations, delirium and coma).*

Walshe JM. Penicillamine, a new oral therapy for Wilson's disease. Am J Med 1956; 21: 487-95. PubMed PMID: 13362281.

*(Initial studies on efficacy of oral penicillamine [ $\beta,\beta$ -dimethyl cysteine, a monothiol] in inducing cupruresis in Wilson disease, and lack of effect of cysteine and methionine; no toxic reactions were observed).*

Vilensky JA, Redman K. British anti-Lewisite (dimercaprol): an amazing history. Ann Emerg Med 2003; 41: 378-83. PubMed PMID: 12605205.

*(History of development and use of dimercaprol, initially synthesized at Oxford during WWII as a means of reversing Lewisite arsenical gas poisoning [thus British anti-Lewisite (BAL)] and now still used for emergency therapy of heavy metal poisoning by arsenic, gold, copper and mercury).*

Ala A, Walker AP, Ashkan K, Dooley JS, Schilsky ML. Wilson's disease. Lancet 2007; 369 (9559): 397-408. PubMed PMID: 17276780.

*(Review of the clinical features, pathogenesis, genetics, diagnosis and treatment).*

Roberts EA, Schilsky ML, AASLD. Diagnosis and treatment of Wilson disease: an update. *Hepatology* 2008; 47: 2089-111. PubMed PMID: 18506894.

*(Thorough review of the cause, natural history, diagnosis and treatment of Wilson disease with specific recommendations for use of penicillamine, trientine and zinc).*

Walshe JM. The conquest of Wilson's disease. *Brain* 2009; 132 (Pt 8): 2289-95. PubMed PMID: 19596747.

*(History of the initial description of Wilson disease, its link to copper accumulation, and therapies several of which were developed by the author).*

Weiss KH, Stremmel W. Evolving perspectives in Wilson disease diagnosis: treatment and monitoring. *Curr Gastroenterol Rep* 2012; 14: 1-7. PubMed PMID: 22083169.

*(Review of the diagnosis and management of Wilson disease, including the role of genetic testing and the choice of medical therapies).*

Breuer C, Oh J, Nolkemper D, Achilles EG, Fischer L, Eglite I, Guesmer C, Heitland P, et al. Successful detoxification and liver transplantation in a severe poisoning with a chemical wood preservative containing chromium, copper, and arsenic. *Transplantation* 2015; 99: e29-30. PubMed PMID: 25827325.

*(4 year old boy ingested wood preservative [chromium, copper and arsenic] and presented with nausea and vomiting followed by renal and hepatic failure, requiring parenteral dimercaprol before and for 3 months after liver transplantation).*

Chakor RT, Bharote H, Eklare N, Tamboli K. Unilateral rubral tremors in Wilson's disease treated with dimercaprol. *Ann Indian Acad Neurol* 2015; 18: 115-6. PubMed PMID: 25745328.

*(22 year old man with Wilson disease and severe tremors not relieved by penicilliamine, responded within a month to a course of dimercaprol; no mention of ALT levels or liver injury).*

Permar S, Gorman K, Lercher D, Bradford KK. Rare etiology of abdominal pain in an adolescent female. *Clin Pediatr (Phila)* 2015; 54: 94-7. PubMed PMID: 25015930.

*(16 year old female developed abdominal pain, hematemesis, anemia and liver test abnormalities [bilirubin 1.4 mg/dL, ALT 81 U/L, AST 70 U/L, Alk P 55 U/L, hematocrit 26.8% with basophilic stippling], found to have lead poisoning from drinking out of locally made terra cotta pottery bought in Mexico; treated with dimercaprol and EDTA).*

Shumy F, Anam AM, Kamruzzaman AK, Amin MR, Chowdhury MA. Acute arsenic poisoning diagnosed late. *Trop Doct* 2016; 46: 93-6. PubMed PMID: 26508422.

*(17 year old Indian man developed nausea, vomiting and progressive flacid paralysis followed by jaundice and coma [bilirubin 10.3 mg/dL, ALT 160] due to arsenic poisoning, responding with slow improvement to a 10 day course of dimercaprol).*

Grasso IA, Blattner MR, Short T, Downs JW. Severe systemic lead toxicity resulting from extra-articular retained shrapnel presenting as jaundice and hepatitis: a case report and review of the literature. *Mil Med* 2017; 182: e1843-e1848. PubMed PMID: 28290970.

*(31 year old soldier with history of gunshot wound developed abdominal pain and jaundice, but normal ALT levels despite liver biopsy showing steatohepaittis; evaluation of anemia demonstrated lead poisoning, that responded partially to several courses of dimercaprol, but eventually required surgical removal of shrapnel in leg).*