DMSA

meso2,3 dimer captosuccinic acid

--- INDICATIONS AND USAGE ---

Chelating agent used for the treatment of heavy metal toxicity, particularly for Arsenic, Cadmium, Lead, and Mercury. It is notably used for poisoning in pediatric patients with blood lead concentrations greater than 45 mg/dL. It is not a substitute for abatement of heavy metal exposure.

--- DOSAGE & ADMINISTRATION ---

For the treatment of lead toxicity secondary to serum lead concentrations above 45 mcg/dL. Oral dosage Adults 30 mg/kg/day PO administered as 5-day treatment courses separated by rest periods of 7 to 10 days has been evaluated in adults. In a study of adults with occupational lead exposure resulting in blood lead concentrations of at least 40 mcg/dL and a positive edetate calcium disodium lead mobilization test, 1,050 mg/m2/day (approximately 30 mg/kg/day) was administered in 3 divided doses over two 5-day courses separated by a 10-day rest period. Another study administered 30 mg/kg/day as a series of 5-day courses separated by at least 1 week to adults with blood lead concentrations of 50 mcg/dL or higher. For pediatric patients, a maximum daily dose of 1,500 mg is recommended by the FDA for patients weighing more than 45 kg.

CHILDREN AND ADOLESCENTS

10 mg/kg/dose or 350 mg/m2/dose PO every 8 hours for the first 5 days, then reduce dosing frequency to every 12 hours for 14 days (total course = 19 days). Max: 1,500 mg/day. Adjust weight-based dose to available practical dose strength: weight 8 to 15 kg = 100 mg/dose; weight 16 to 23 kg = 200 mg/dose; weight 24 to 34 kg = 300 mg/dose; weight 35 to 44 kg = 400 mg/dose; weight more than 45 kg = 500 mg/dose. Repeat courses may be necessary based upon weekly monitoring of blood lead concentrations. Wait at least 2 weeks in between courses of therapy unless blood lead concentrations indicate the need for prompt treatment.

MAXIMUM DOSAGE

Adults
30 mg/kg/day PO has been evaluated for off label use.

Geriatric
30 mg/kg/day PO has been evaluated for off label use

Adolescents

More than 45 kg	500 mg/dose PO
35 to 44 kg	400 mg/dose PO
24 to 34 kg	300 mg/dose PO
16 to 23 kg	200 mg/dose PO
8 to 15 kg	100 mg/dose PO

Children

More than 45 kg	500 mg/dose PO
35 to 44 kg	400 mg/dose PO
24 to 34 kg	300 mg/dose PO
16 to 23 kg	200 mg/dose PO
8 to 15 kg	100 mg/dose PO

Infants
Safety and efficacy have not been established.

Neonates
Safety and efficacy have not been established.

--- DOSAGE CONSIDERATIONS ---

Hepatic Impairment
Specific guidelines for dosage adjustments in hepatic impairment are not available; it appears that no dosage adjustments are needed. No data are available regarding the metabolism of DMSA in patients with hepatic impairment. Closely monitor patients with a history of hepatic disease, as transient mild elevations in serum transaminases have occurred during treatment.

--- DOSAGE & ADMINISTRATION ---

Renal Impairment
Specific guidelines for dosage adjustments in renal impairment are not available; it appears that no dosage adjustments are needed. Use with caution in patients with renal impairment. Intermittent hemodialysis Limited data suggest that DMSA is dialyzable, but lead chelates are not.

--- DOSAGE FORMS & STRENGTHS ---

Available in manufactured 100mg capsules, and compounded as a powder, liquid suspension, or suppository.

--- CONTRAINDICATIONS ---

1. Allergy or Sensitivity: If there is a known allergy or sensitivity to DMSA, or any of its components, it should not be used. Allergic reactions can be severe and life-threatening.
2. Severe Renal Impairment: DMSA is primarily excreted through the kidneys. If severe kidney impairment or renal failure exists, dosages should be adjusted and alternative treatments should be considered. DMSA can accumulate in the body.
3. If risk of neutropenia (absolute neutrophil count (ANC) is below 1200/mcL).

WARNINGS & PRECAUTIONS

Keep out of reach of pediatric patients. DMSA is not a substitute for effective abatement of lead exposure.

Patients should be instructed to promptly report any indication of infection, which maybe a sign of neutropenia.

--- ADVERSE REACTIONS & POSSIBLE SIDE EFFECTS ---

Although DMSA is known to be a safe agent when used in correct clinical settings, there have been reports of GI upsets, skin reactions, mild neutropenia, and elevated liver enzymes. A rare side effect reported is mucocutaneous eruptions and toxic epidermal necrosis that resolves when DMSA is discontinued.

Mild to moderate neutropenia has been observed in some patients receiving DMSA. While a causal relationship to DMSA has not been definitely established, neutropenia has been reported with other drugs in the same chemical class. A complete blood count with white blood cell differential and direct platelet counts should be obtained prior to and weekly during treatment with DMSA. Therapy should either be withheld or discontinued if the absolute neutrophil count (ANC) is below 1200/mcL and the patient followed closely to document recovery of the ANC to above 1500/mcL or to the patient's baseline neutrophil count.

Severe

Proteinuria Delayed	0-3.7
Angioedema Rapid	0-1.0 a
Arrhythmia exacerbation Early	0-1.0

Moderate

Candidiasis Delayed	5.2-15.7
Flank pain Delayed	5.2-15.7
Hypercholesterolemia Delayed	4.2-10.4
Elevated hepatic enzymes Delayed	4.2-10.4
Hemorrhoids Delayed	1.0-10.0
Peripheral neuropathy Delayed	1.0-10.0
Oral ulceration Delayed	1.0-10.0
Dysuria Early	0-3.7
Urinary retention Early	0-3.7
Neutropenia Delayed	0-1.0
Thrombocytosis Delayed	0-1.0
Eosinophilia Delayed	0-1.0

Mild

Chills Rapid	5.2-15.7
Abdominal pain Early	5.2-15.7
Headache Early	5.2-15.7
Fever Early	5.2-15.7
Back pain Delayed	5.2-15.7
Fatigue Early	5.2-15.7
Pruritus Rapid	2.6-11.2
Anorexia Delayed	1.0-10.0
Dizziness Early	1.0-10.0
Paresthesias Delayed	1.0-10.0
Irritability Delayed	1.0-10.0
Maculopapular rash Early	1.0-10.0
Vesicular rash Delayed	1.0-10.0
Rash Early	4.0-4.0
Cough Delayed	0.7-3.7
Nasal congestion Early	0.7-3.7
Throat irritation Early	0.7-3.7
Rhinorrhea Early	0.7-3.7
Lacrimation Early	1.0-3.7
Infection Delayed	0-1.0
Urticaria Rapid	0-1.0
Diarrhea Early	10.0
Metallic taste Early	10.0
Nausea Early	10.0
Vomiting Early	10.0
Drowsiness Early	10.0

DRUG INTERACTIONS

Edetate Calcium Disodium, Calcium EDTA: (Moderate) Concomitant use of DMSA and other chelation therapy such as edetate calcium disodium, calcium EDTA (CaNa2EDTA) with or without dimercaprol (BAL) is not recommended, as data are not available. Patients who have received CaNa2EDTA with or without dimercaprol may use DMSA for subsequent treatment after an interval of 4 weeks.

MECHANISM OF ACTION

DMSA is an orally administered lead chelator. The sulfhydryl, or thiol, groups of DMSA bind with lead to form water-soluble chelates, which are excreted in the urine. DMSA lowers blood lead concentrations. For example, among adults with blood lead concentrations of 44 to 96 mcg/dL who received oral DMSA, the mean lead blood concentrations decreased 72.5% after 5 days of 10 mg/kg orally every 8 hours, 58.3% after 5 days of 6.7 mg/kg every 8 hours, and 35.5% after 5 days of 3.3 mg/kg every 8 hours. In the initial 24 hours after receipt of the 10 mg/kg dose, the mean urinary excretion of lead was 28.6-times the pretreatment 24-hour urinary lead excretion. As the chelatable pool was reduced during treatment, urinary lead output decreased. In addition to adults, DMSA also lowers blood lead concentrations in children. Among children 2 to 7 years of age who received 350 mg/m2 every 8 hours for 5 days, the mean blood lead concentration decreased 78%. Unfortunately, both adults and pediatric patients experienced a rebound in blood lead concentrations after DMSA discontinuation. For example, after receipt of 350 mg/m2 (10 mg/kg) every 8 hours for 5 days, the mean lead concentration rebounded and plateaued at 60% to 85% of pretreatment concentrations 2 weeks after therapy. DMSA receipt beyond 5 days was studied to examine the effect of longer dosing on the rebound of blood lead concentrations. Children 1 to 7 years of age with blood lead concentrations of 42 to 67 mcg/dL who received 350 mg/m2 every 12 hours for 2 weeks after the initial 5 days of 350 mg/m2 every 8 hours did not experience rebound of blood lead concentrations after the initial 5-day treatment period. Further, less rebound was noted after DMSA discontinuation. In another study, 10 children aged 21 to 72 months with blood lead concentrations of 30 to 57 mcg/dL received DMSA 350 mg/m2 by mouth every 8 hours for 5 days, followed by 350 mg/m2 by mouth every 12 hours for an additional 19 to 22 days. Blood lead concentrations decreased and remained stable under 15 mcg/dL during the extended dosing period. DMSA is indicated for a total therapy duration of 19 days, and additional treatment courses may be needed. DMSA is an effective chelator with minimal effect on the excretion of essential minerals when compared to edetate calcium disodium, calcium EDTA (another medication used for the treatment of lead toxicity). Treatment with DMSA results in a doubling in zinc excretion but does not have a significant effect on the urinary elimination of iron, calcium, or magnesium.

PHARMACOKINETICS

DMSA is administered orally. After 10 mg/kg of DMSA was administered orally to healthy adults, DMSA was rapidly and extensively metabolized. Approximately 25% of the dose was excreted in the urine, with peak blood concentration and urinary excretion occurring between 2 and 4 hours. Only 10% of DMSA excreted in the urine was excreted as unchanged drug. The majority of drug excreted in the urine occurred as mixed DMSA-cysteine disulfides.

Affected cytochrome P450 isoenzymes: none

ORAL ROUTE

In a study of healthy volunteers, after the administration of a single dose of radiolabeled DMSA, absorption was rapid but variable with peak blood radioactivity concentrations occurring within 1 to 2 hours after administration. Pregnancy And Lactation Pregnancy DMSA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. There are no adequate and well-controlled studies in pregnant women; however, the drug has been found to be teratogenic and fetotoxic in pregnant mice.[PDR 2023 15142] Exposure to lead can be a concern for maternal and fetal harm. Per CDC current guidelines, the essential actions for managing pregnant women with blood lead levels of 5 mcg/dL or more are removal of the lead source, disruption of the route of exposure, and avoidance of the lead-containing substance or activity. In circumstances where the maternal blood lead concentration is 45 mcg/dL or more, chelation therapy may be warranted after consultation with an expert in lead poisoning and perinatologists; for lower lead concentrations, data are insufficient to advise the use of chelation during pregnancy. Avoid chelation during the first trimester in all pregnant women, unless the lead intoxication is severe (maternal lead encephalopathy), due to the general concerns of drug use during organogenesis. Although no chelation-attributable toxicities have been reported in the existing published case reports of the treatment of pregnant women, very limited information is available to understand any potential short- or long-term effects for the fetus.[PDR 2023 49776] It is not known if DMSA is excreted in human breast milk. Because many drugs and heavy metals are excreted in human milk, lactating mothers requiring DMSA therapy should be discouraged from nursing infants.[PDR 2023 15142] According to CDC guidelines, the risk of adverse developmental effects in infants with blood lead concentrations of 5 mcg/dL or more is of greater concern than the risks associated with not breast-feeding. Thus, the CDC encourages mothers with blood lead concentrations of 40 mcg/dL or more to pump and discard their breast milk until their blood lead levels drop below 40 mcg/dL. These recommendations are made for the US population and may not be appropriate for other countries, where infant mortality from other causes is a greater concern.

Information sourced from PDR 2023 and PubMed. Information about suppository dosing provided by PharmaChelation.com