PRIOR AUTHORIZATION POLICY

POLICY: Chelating Agents – Chemet Prior Authorization Policy
- Chemet® (succimer capsules – Lannett/Recordati Rare Diseases)

REVIEW DATE: 01/29/2025

OVERVIEW

Chemet, a heavy metal chelator, is indicated for the treatment of **lead poisoning** in pediatric patients ≥ 1 year of age with blood lead levels > 45 mcg/dL.[1] Limitations of Use: Chemet is not indicated for prophylaxis of lead poisoning in a lead-containing environment. Chemet does not cross the blood-brain barrier and is not indicated to treat encephalopathy associated with lead toxicity. Safety and efficacy of Chemet in children < 12 months of age have not been established. The course of therapy is 19 days. If indicated, a repeat course may be given with a minimum of 2 weeks between courses, unless blood lead levels indicate the need for more prompt treatment. The chemical name for Chemet is *meso* 2,3-dimercaptosuccinic acid (DMSA).

Disease Overview

Lead, mercury, arsenic, and iron account for most cases of diagnosed heavy metal poisoning in the US.[2] Most cases of lead poisoning are in children who swallow lead-based paint in homes or toys; other causes include water carried through pipes made of lead or containing lead solder. Children are especially susceptible to the toxic effects of lead, which may affect the developing brain and nervous system, potentially causing lower IQs, learning difficulties, hearing loss, and behavior difficulties. In adults, lead poisoning can cause high blood pressure and kidney damage.

Treatment Recommendations

Treatment of heavy metal poisoning includes removing the patient from the source of the metal and treating the patient's symptoms.[2] Diagnosis includes the patient's history, symptoms, and blood or urine tests.[2,4,5] Treatment of acute metal poisoning involves emergency care and generally requires the use of chelating agents, such as DMSA.[6]

Other Uses with Supportive Evidence

Arsenic is a naturally-occurring substance; in some areas of the world, low-level arsenic exposure occurs because of the presence of arsenic in ground water.[2] Accidental poisoning accounts for the majority of acute arsenic toxicity.[3] The Agency for Toxic Substances and Disease Registry (ATSDR) states that patients with severe arsenic poisoning must be hospitalized.[7] Chelation therapy can curtail the distribution of arsenic in the body and reduce the body burden. Oral chelators, such as Chemet, have been used with success. There are case reports to support the use of DMSA in acute arsenic poisoning.[3,8] The patients' clinical status improved with DMSA therapy and urine arsenic levels decreased with therapy. Note: The chemical name, DMSA, may be used to describe the case reports in this document because it is unclear if the FDA-approved Chemet product was used.

Mercury poisoning can result from vapor inhalation, mercury ingestion, mercury injection, and absorption of mercury through the skin.[5] Symptoms of mercury poisoning depends on the type of mercury exposure and severity of exposure: organic mercury (antiseptics, bactericidals, fungicides, insecticides), inorganic mercury (chemical laboratory work, disinfectants, explosives, fur hat processing), and elemental mercury (thermometers, batteries, dental amalgams, fluorescent lamps). The ATSDR notes that patients with serious mercury exposure must be hospitalized.[9] Chelation should be considered for any symptomatic patient with a clear history of acute elemental mercury exposure. The decision to chelate is less clear in asymptomatic

patients with elevated urine mercury levels.[10] Oral chelators, such as Chemet, have been used successfully for the treatment of acute mercury intoxication/poisoning.[9] The World Health Organization (WHO) recommends that urine mercury concentration should not exceed 50 mcg/g creatinine.[11]

Several case reports have demonstrated the effectiveness of DMSA therapy for treatment of acute mercury poisoning.[12-15] All of the patients exhibited symptoms consistent with mercury poisoning and were treated in a hospital setting. DMSA therapy resulted in reduction of mercury levels and improved symptomatology.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Chemet. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Chemet as well as the monitoring required for adverse events, approval requires Chemet to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required for use of Chemet as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, prescription claims records, prescription receipts and/or other information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Chemet is recommended in those who meet one of the following criteria:

FDA-Approved Indication

1. **Acute Lead Poisoning.** Approve for 2 months if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient is between the age of 12 months and 18 years of age; AND
   - **B)** Prior to starting Chemet therapy, the patient's blood lead level was > 45 mcg/dL **[documentation required]**; AND
   - **C)** Chemet is being used for treatment of acute lead poisoning and not as prophylaxis against lead poisoning in a lead-containing environment; AND
   - **D)** The medication is prescribed by or in consultation with a professional experienced in the use of chelation therapy (e.g., a medical toxicologist or a poison control center specialist).

Other Uses with Supportive Evidence

2. **Acute Arsenic Intoxication/Poisoning.** Approve for 1 month if the patient meets BOTH of the following (A and B):
   - **A)** Patient was recently initiated on Chemet therapy in the hospital and further treatment is needed to finish the course of therapy; AND
   - **B)** The medication is prescribed by or in consultation with a professional experienced in the use of chelation therapy (e.g., a medical toxicologist or a poison control center specialist).

A) Patient was recently initiated on Chemet therapy in the hospital and further treatment is needed to finish the course of therapy; AND
B) The medication is prescribed by or in consultation with a professional experienced in the use of chelation therapy (e.g., a medical toxicologist or a poison control center specialist).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Chemet is not recommended in the following situations:

1. **Concomitant Use with Other Chelators (e.g., calcium disodium versenate injection [$CaNa_2EDTA$], dimercaprol injection [British anti-Lewisite {BAL}]).**
   In patients with acute lead poisoning, data on the concomitant use of Chemet with $CaNa_2EDTA$ with or without BAL are not available and such use is not recommended.[1] Patients who have received $CaNa_2$ EDTA with or without BAL may use Chemet for subsequent treatment after an interval of 4 weeks.

2. **Chelation of Heavy Metals to Treat Chronic Medical and/or Psychiatric Conditions.** Chelation of heavy metals has been advertised as a viable treatment for numerous conditions: treatment of intermittent claudication; treatment or management of symptoms of autism; prevention or cure of neurodegenerative conditions such as Alzheimer's disease; use in Parkinson's disease; treatment of macular degeneration.[2] There is no evidence to show that chelators work in these conditions. Furthermore, unapproved uses of chelation therapy have resulted in harm and even death. Chelation of heavy metals is also one of several popular interventions in children with autism spectrum disorders. The FDA notes chelation therapies for the treatment of autism to be associated with significant health risks and does not approve such use.[16]

3. **Chronic Arsenic Exposure.** Use of chelation therapy following chronic exposure to inorganic arsenic may accelerate metal excretion, but potential therapeutic efficacy in terms of decreased morbidity and mortality is largely unestablished.[17]

   In a prospective, randomized-controlled trial, 21 patients with chronic arsenicosis due to drinking arsenic-contaminated subsoil water were randomized to receive DMSA (1,400 mg/day or 100 mg/m^2 in four divided doses for 1 week and then 1,050 mg/day or 750 mg/m^2 in three divided doses for 2 weeks; repeat the regimen after 3 weeks) or placebo.[18] The patients had of drinking arsenic-contaminated water (50 mcg/L or $\geq$ 0.05 mg/L) for at least 2 years and exhibited clinical signs/symptoms of chronic arsenicosis. Similar improvement in the clinical score was observed in the DMSA and placebo groups. Furthermore, urinary arsenic excretion before treatment and at 48 hours and 72 hours post-treatment were similar between the two groups. The investigators concluded that DMSA did not result in clinical or biochemical benefit in patients with chronic arsenicosis.

   In another case report involving a 39 year old woman with arsenic poisoning (urine arsenic level was 2,000 mcg/L; normal level is < 10 mcg/L), DMSA 600 mg three times a day for 45 days did not significantly affect the clearance of arsenic or clinical outcome.[19] During the 45-day course, the patient stopped therapy for a total of 13 days (unknown reason).

4. **Chronic Mercury Exposure.** The American Academy of Pediatrics notes there is no scientific evidence behind the use of chelation therapy to improve nervous system symptoms of chronic mercury toxicity.[16] Use of chelation therapy following chronic exposure to inorganic mercury may accelerate metal excretion, but potential therapeutic efficacy in terms of decreased morbidity and mortality is largely unestablished.[17]

In a randomized, double-blind, parallel-group, placebo-controlled study in Sweden, 20 patients were randomized to receive DMSA 20 mg/kg/day in three divided doses or placebo for 14 days.[20] These patients experienced symptoms that were allegedly associated with amalgam fillings for at least 6 months. DMSA therapy resulted in increased urinary excretion of mercury and blood mercury levels were decreased. However, there were no statistically significant changes in any of the symptoms. The investigators concluded that although urinary excretion of mercury was increased during DMSA treatment, chelating therapy did not alleviate symptoms allegedly attributable to mercury from amalgam fillings.

Cao and colleagues reported the effects of Chemet in reducing blood mercury levels in children 12 to 33 months of age.[21] The original study was to evaluate the use of Chemet for lead poisoning; the investigators used the blood samples for the lead study and measured the mercury levels. Blood mercury concentrations were measured 1 week before randomization and treatment, at 1 week after treatment initiation, and after three courses of treatment. Mercury was not detected/quantified in any of the blood samples. At 1 week of treatment, organic mercury concentration decreased 8% in the Chemet group, but remained the same in the placebo group (P = 0.04). However, the investigators suggested that the difference was not due to a reduction in the Chemet group but rather, Chemet therapy prevented a rise in the blood mercury concentration as seen in the placebo group. Chemet therapy did not reverse the accumulation of organic mercury over multiple courses over 5 months.

5. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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