Chelation therapy is unproven and not medically necessary for treating "mercury toxicity" from dental amalgam fillings. Randomized controlled trials do not identify a causal association between amalgam fillings and various systemic symptoms and disorders attributed to mercury.

Chelation therapy is unproven and not medically necessary for treating chronic, progressive diseases (not involving heavy metal toxicity or overload conditions) and other disorders including but not limited to:

- Alzheimer's disease
- Apoplectic coma
- Autism spectrum disorder
- Cancer
- Cardiovascular disease
- Chronic fatigue syndrome
- Chronic renal insufficiency
- Defective hearing
- Diabetes
- Diabetic ulcer
- Cholelithiasis
- Gout
- Erectile dysfunction
- Multiple sclerosis
- Osteoarthritis
- Osteoporosis
- Parkinson's disease
- Raynaud's disease
- Renal calculus
- Rheumatoid arthritis
- Schizophrenia
- Scleroderma
- Snake venom poisoning
- Varicose veins
- Vision disorders (glaucoma, cataracts, etc.)

Much of the evidence supporting chelation treatment for other chronic progressive disease is based on testimonials and single-case studies. Thus, there still is no scientific evidence that demonstrates any benefit from this form of therapy.
Chelation Therapy for Non-Overload Conditions

UnitedHealthcare Commercial Medical Policy

Effective 11/01/2018

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APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>J3490</td>
<td>Unclassified drugs</td>
</tr>
<tr>
<td>M0300</td>
<td>IV chelation therapy (chemical endarterectomy)</td>
</tr>
<tr>
<td>S9355</td>
<td>Home infusion therapy, chelation therapy; administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem</td>
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</table>

DESCRIPTION OF SERVICES

Chelation therapy involves the administration of naturally occurring or chemically designed molecules to bind and excrete a specific toxin in the body. The specific medication, route, method and site of administration of the chelating agent varies depending on the specific agent used, the level of toxicity, and other clinical indications. Heavy metal toxicity most often treated with chelation therapy includes that caused by iron, copper, lead, aluminum, and mercury.

Non-Overload Conditions

Chelation therapy has been proposed as a treatment for a variety of non-overload conditions in which the removal of heavy metal ions is hypothesized to reduce oxidative damage caused by the production of hydroxyl radicals. However, the possible mechanism of chelators as therapeutic agents for non-overload conditions is not fully understood. Chelation has been investigated as a treatment of numerous non-overload conditions including, but not limited to, cardiovascular disease, rheumatoid arthritis (RA), cancer, and diabetes.

Mercury Poisoning

Chelation therapy has been proposed to treat metal toxicity from dental amalgam fillings, but it has not been shown that mercury amalgams cause harm to individuals with dental fillings, except in rare cases of allergy.

CLINICAL EVIDENCE

Non-Overload Conditions

Well-designed, published and peer-reviewed studies do not support chelation treatment for chronic, progressive diseases such as cardiovascular disease, atherosclerosis, diabetes, cancer, Alzheimer's disease, autism spectrum disorder, or RA. There are no studies available regarding chelation therapy for the treatment of apoplectic coma, chronic fatigue syndrome, chronic renal insufficiency, defective hearing, diabetic ulcer, cholelithiasis, gout, erectile dysfunction, multiple sclerosis, osteoarthritis, osteoporosis, Parkinson's disease, Raynaud's disease, renal calculus, schizophrenia, scleroderma, snake venom poisoning, varicose veins, or vision disorders. There is insufficient evidence that chelation therapy is safe and effective to remove other undesirable metabolites or toxins, or have a positive impact on clinical outcomes for other disease states.

Alzheimer's Disease (AD)

Increased levels of aluminum have been discovered in several brain regions of individuals with AD. Epidemiological studies have linked the concentration of aluminum in drinking water and the increased occurrence of the disease. Scientists have postulated that chelation therapy might promote beneficial results in AD patients by inhibiting the deposition of aluminum in the brain or by preventing iron from catalyzing the formation of toxic hydroxyl radicals. Aluminum chelators may also reactivate aluminized metalloenzyme complexes in AD patients and permit redistribution of aluminum in the brain.

A Cochrane systematic review was conducted by Sampson et al. to evaluate the efficacy of metal protein attenuating compounds (MPACs) for the treatment of cognitive impairment due to AD. The primary outcome measure was cognitive function (measured by psychometric tests). Two MPAC trials were identified. One trial compared clioquinol (PBT1) with placebo in 36 patients and 32 had sufficient data for per protocol analysis. There was no statistically significant difference in cognition (as measured on the Alzheimer's Disease Assessment Scale-Cognition (ADAS-Cog)) between the active treatment and placebo groups at 36 weeks, and there was no significant impact on non-cognitive symptoms or clinical global impression. In the second trial a successor compound, PBT2, was compared with placebo...
Chelation therapy has been proposed as a treatment of coronary artery disease, based in part on the hypothesis that chelation could remove atherosclerotic calcium deposits or provide an antioxidant benefit.

In November 2012, the American Heart Association (AHA) announced preliminary results of the Trial to Assess Chelation Therapy (TACT). TACT was a multicenter, double-blind, randomized efficacy trial that took place from 2002 to 2011. Patients (n=1700) were randomized to receive 40 infusions of a 500-mL chelation solution or a placebo infusion, with a second randomization to an oral vitamin and mineral regimen or an oral placebo. Each patient received 40 infusions, each lasting at least 3 hours. Researchers found that patients receiving the chelation solution had fewer serious cardiovascular events than the control group: 26% versus 30%. Cardiovascular events were defined as death, heart attack, stroke, coronary revascularization, and hospitalization for angina. Because the level of statistical difference between the groups was small, it is not known whether the effect will be reproducible in a real-world scenario. Investigators cautioned that the results need to be reproduced and understood before consideration of clinical application.

Further analysis of the TACT data by Lamas et al. (2013) reported that in stable patients with a history of myocardial infarction (MI), the use of an intravenous chelation regimen with Edetate calcium disodium (EDTA) modestly reduced the risk of a variety of adverse cardiovascular outcomes compared to placebo. The authors stated that while these results should guide further research, there still is not sufficient evidence to support routine use of chelation therapy in post-MI patients.

Using the TACT data, an initial subgroup analysis showed a greater effect of EDTA treatment among participants with a self-reported history of diabetes. Further examination of the data in patients with diabetes demonstrated a 41% overall reduction in the risk of any cardiovascular event; a 40% reduction in risk of cardiovascular mortality, non-fatal stroke, or non-fatal MI; a 52% reduction in recurrent heart attacks; and a 43% reduction in death from any cause. In contrast, there was no significant benefit of EDTA treatment in the subgroup of 1,045 participants who did not have diabetes. The authors note that results of this analysis support the initiation of clinical trials in patients with diabetes and vascular disease to replicate these findings, and to define the mechanisms of benefit. However, it was also concluded that there is not enough evidence to support the routine use of chelation therapy for this population (Escolar et al. 2013).
Trial to Assess Chelation Therapy 2 (TACT2) is a randomized, double blind controlled factorial clinical trial of edetate disodium-based chelation and high-dose oral vitamins and minerals to prevent recurrent cardiac events in diabetic patients with a prior MI. This study is currently recruiting participants. Additional information is available at www.clinicaltrials.gov.

**Rheumatoid Arthritis**

In a review of chelation for non-overload conditions, Voest et al. (1994) summarized the available literature regarding RA. In 6 small studies with patient populations ranging from 6 to 18 patients, deferoxamine improved the clinical symptoms and reduced anemia in the majority of patients. However, the authors concede that the preponderance of evidence regarding chelation for RA is derived from small numbers of patients treated for a short amount of time. The authors assert that larger studies are needed to determine the role of iron chelators in the treatment of RA.

In a second review, Ghio et al. (1997) hypothesized that iron chelation may play a vital role in reducing neutrophilic inflammation. Thus, these investigators also contend that additional trials of iron chelation for RA are warranted.

**Professional Societies**

**American Academy of Family Physicians (AAFP)**

The AAFP endorses the 1983 American Medical Association (AMA) Diagnostic and Therapeutic Assessment of Chelation Therapy which states, “Chelation therapy with ethylene diamine tetraacetic acid or its sodium salt is not an established treatment for atherosclerotic vascular disease” (2013).

**American College of Cardiology (ACC)**

The ACC concluded that although disodium EDTA is approved by the U.S. Food and Drug Administration for specific indications, such as iron overload and lead poisoning, it is not approved for use in preventing or treating cardiovascular disease. Accordingly, the group finds that the usefulness of chelation therapy in cardiac disease is highly questionable (Fihn et al. 2014).

**American College of Physicians (ACP)**

A clinical practice guideline published by the ACP recommended against the use of chelation therapy to prevent MI or to reduce symptomatic angina (Snow et al. 2004).

**Mercury Poisoning**

Randomized controlled trials have concluded that mercury amalgams used in dental restorations cause no harm to patients. (Shenker et al., 2008; Bellinger et al., 2006; DeRouen et al., 2006)

Langworth et al. (2002) conducted a study evaluating residents in the Stockholm County area with morbidities attributed to dental fillings (‘amalgam disease’). Participants were referred to a special Amalgam Clinic and received examination by a dentist (n=428), a physician (n=379), and a psychologist (n=360). Gender ratio was 69% women and 31% men and the mean patient age was 46 years. No positive correlation was found between the amount of amalgam and somatic symptoms or psychological effect parameters. The authors concluded that the data gathered did not support the hypothesis that release of mercury from amalgam fillings is the cause of ‘amalgam disease’, but suggest that there may be various explanations for the patients’ complaints.

**Professional Societies**

**American Cancer Society (ACS)**

The ACS stated that chelation therapy is a proven treatment for lead poisoning and poisoning from other heavy metals. However, available scientific evidence does not support claims that the treatment benefits patients with cancer, heart disease, or any medical problems other than heavy-metal poisoning (2014).

**American Dental Association (ADA)**

The ADA website contains statements from a number of organizations that there is no known association between dental amalgam and a specific disease. Examples of these organizations include but are not limited to:

- Alzheimer's Association
- Lupus Foundation of America
- Mayo Clinic
- National Multiple Sclerosis Society

**U.S. FOOD AND DRUG ADMINISTRATION (FDA)**

Edetate calcium disodium, also called EDTA is approved for the treatment of lead poisoning in adults and children.
Desferal which is the trade name for DFO (deferoxamine mesylate, deferoxamine B mesylate, deferoxamine, desferroxamine, desferrioxamine) and Jadenu (deferasirox) are FDA-approved chelators for iron overload.

Dimercaprol (BAL oil) is also approved for the heavy metal chelation of iron. Deferiprone (Ferriprox) is FDA approved for the treatment of iron overload in patients with hematologic disorders requiring chronic transfusion therapy.

Additional information is available at: http://www.accessdata.fda.gov/scripts/Cder/ob/default.cfm.
(Accessed January 19, 2018)

The FDA reaffirmed its position that amalgam is a safe and effective dental material after thoroughly reviewing the current science and updating its consumer advisory on dental amalgam fillings. Additional information is available at: http://www.ada.org/en/press-room/news-releases/2015-archive/january/fda-updates-consumer-advisory.
(Accessed January 19, 2018)

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not cover chelation therapy for non-overload conditions. Refer to the National Coverage Determinations (NCDs) for Chelation Therapy for Treatment of Atherosclerosis (20.21) and Ethylenediamine-Tetra-Acetic (EDTA) Chelation Therapy for Treatment of Atherosclerosis (20.22). Local Coverage Determinations (LCDs) do not exist at this time.
(Accessed January 23, 2018)

REFERENCES


**POLICY HISTORY/REVISION INFORMATION**

<table>
<thead>
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<th>Action/Description</th>
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| 11/01/2018| - Reorganized policy template:  
  - Simplified and relocated Instructions for Use  
  - Removed Benefit Considerations section  
  - Updated coverage rationale; modified language to clarify the listed services are:  
    - Proven and medically necessary (as described)  
    - Unproven and not medically necessary (as described)  
  - Archived previous policy version 2018T0051Q |

**INSTRUCTIONS FOR USE**

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. UnitedHealthcare Medical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.