

# Chelation Therapy for Non-Overload Conditions (for North Carolina Only)

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[Instructions for Use](#)

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Related Policies
None

## Application

This Medical Policy only applies to the state of North Carolina.

## Coverage Rationale

Chelation for heavy metal toxicity and overload conditions (e.g., iron, copper, lead, aluminum) is proven and medically necessary and not addressed in this policy.

The following are unproven and not medically necessary due to insufficient evidence of efficacy:

- Chelation therapy for treating any chronic, progressive diseases associated with [non-overload conditions](#)
- Chelation therapy for treating mercury “toxicity” from dental amalgam fillings

## 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 federal, state, or contractual requirements 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 Guidelines may apply.

HCPCS Code	Description
J0470	Injection, dimercaprol, per 100 mg
J0600	Injection, edetate calcium disodium, up to 1000 mg
J0895	Injection, deferoxamine mesylate, 500 mg
J3490	Unclassified drugs

HCPCS Code	Description
J8499	Prescription drug, oral, nonchemotherapeutic, NOS
M0300	IV chelation therapy (chemical endarterectomy)
S9355	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

## Description of Services

Chelation therapy can provide substantial clinical benefit for conditions where heavy metal overload has been accurately diagnosed. The diagnostic workup must consider the individual's history, an appropriate choice of testing methods, and the use of accurate and specific reference values. Chelation therapy is an established treatment for the removal of metal toxins from the body. This 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, where acute or chronic heavy metal toxicity has not been demonstrated, and 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 "Toxicity" from Dental Amalgam Fillings

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. No quality peer-reviewed studies were identified 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. Some 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 aluminum 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 AD 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 in 78 participants with mild AD. There was no significant difference in the Neuropsychological Test Battery (NTB) composite or memory between placebo and PBT2 at week 12. However, two executive function component tests of the NTB showed significant improvement over placebo in the PBT2 250 mg group from baseline to week 12. There was no significant effect on cognition on Mini-Mental State Examination (MMSE) or ADAS-Cog scales. PBT2 did have a favorable safety profile. The authors concluded that there is an absence of evidence as to whether clioquinol (PBT1) is safe or has any positive clinical benefit for patients with AD, and cited that further development of PBT1 has been abandoned. The second trial of PBT2 was more rigorously conducted and appeared to be safe and well tolerated in individuals with mild AD after 12 weeks. Larger trials are now required to demonstrate cognitive efficacy (2014).

Several studies have suggested improvement in cognitive function or biomarkers in patients treated with clioquinol or deferoxamine (Crappier Mclachlan, 1991; Regland, 2001; Ritchie, 2003). However, these studies were small, only two were placebo-controlled, and none were double-blind, and therefore no conclusions regarding the clinical efficacy of chelation therapy for AD can be made on the basis of these studies.

### ***Autism Spectrum Disorder (ASD)***

A National Institute for Health and Care Excellence (NICE) guideline on autism does not recommend the use of chelation for the management of core symptoms of autism in adults (2016, Reaffirmed 2020).

A Cochrane systematic evidence review found no clinical trial evidence to suggest that pharmaceutical chelation is an effective intervention for ASD. One study was found, which was conducted in two phases. During Phase 1, 77 children with ASD were randomly assigned to receive seven days of glutathione lotion or placebo lotion, followed by three days of oral dimercaptosuccinic acid (DMSA). A total of 49 children who were found to be high excretors of heavy metals during Phase 1 continued on to Phase 2 and received three days of oral DMSA or placebo followed by 11 days off, with the cycle repeated up to six times. The second phase assessed the effectiveness of multiple doses of oral DMSA compared with placebo in children who were high excretors of heavy metals and who received a three-day course of oral DMSA. Overall, no evidence suggests that multiple rounds of oral DMSA had an effect on ASD symptoms. The authors concluded that given prior reports of serious adverse events such as hypocalcaemia, renal impairment and reported death, the risks of using chelation for ASD currently outweigh proven benefits. In their opinion, evidence that supports a causal link between heavy metals and autism must be identified and methods that ensure the safety of participants is imperative before further trials are conducted (James, et al. 2015).

### ***Cardiovascular Disease (CVD)***

Chelation therapy has been proposed as a treatment of coronary artery disease (CAD), based in part on the hypothesis that chelation could remove atherosclerotic calcium deposits or provide an antioxidant benefit. The use of chelation therapy in lieu of established therapies, the lack of adequate prior research to verify its effectiveness and clinical utility, and the overall impact of CAD prompted the National Center for Complementary and Alternative Medicine (NCCAM) and the National Heart, Lung, and Blood Institute (NHLBI) to sponsor a large-scale clinical study. This five-year Trial to Assess Chelation Therapy (TACT) in CAD began recruiting individuals in March of 2003.

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=1,700) 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 three 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.

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).

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 findings of the primary outcome barely reached the pre-specified statistical significance level, and therefore the role of chance in these findings is unclear. None of the findings on the secondary outcomes were statistically significant. Therefore, independent replication of the findings would be necessary to consider this treatment as proven. 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.

### ***Rheumatoid Arthritis***

No randomized controlled trials evaluating chelation therapy for rheumatoid arthritis were identified.

### ***Clinical Practice Guidelines***

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

In its clinical policy on chelation therapy, the AAFP states that chelation therapy is appropriate for cases of heavy metal intoxication, when diagnosed using validated testing in appropriate biological samples. The use of chelation therapy for other problems remains investigational and should not be recommended (2018).

#### **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)**

The American College of Physicians, American College of Cardiology Foundation, American Heart Association, and three other medical associations published joint clinical practice guidelines on the management of stable ischemic heart disease (IHD). The guidelines recommended that chelation therapy should not be used with the intent of improving symptoms or reducing cardiovascular risk in patients with stable ischemic heart disease (Qaseem et al., 2012)

In 2004, the American College of Physician's clinical practice guidelines stated that chelation should not be used to prevent myocardial infarction or death or to reduce symptoms in patients with symptomatic chronic stable angina (Snow et al. 2004).

#### **Canadian Cardiovascular Society**

The evidence-based, consensus guidelines (2014) from the Canadian Cardiovascular Society included a conditional recommendation (based on moderate-quality evidence) that chelation therapy should not be used to attempt to improve angina or exercise tolerance in patients with stable ischemic heart disease (IHD) (Mancini et al. 2014).

### **Mercury “Toxicity” from Dental Amalgam Fillings**

Dental amalgams have been investigated as a cause of increased blood levels of mercury, potentially associated with a number of diseases and disorders. While no studies were identified that addressed chelation directly therapy for mercury “toxicity” from amalgam fillings, indirect high-quality evidence support the lack of such toxicity. 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).

## *Clinical Practice Guidelines*

### 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 (March 2019).

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)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Chelation therapy, using FDA-approved chelating agents, is approved when used as a treatment for metal poisoning or iron overload. Use is limited to FDA-approved indications for each chelation agent, as referenced in a generally recognized drug compendium (e.g., American Hospital Formulary Services Drug Information® or DrugDex® System).

Additional information is available at: <http://www.accessdata.fda.gov/scripts/Cder/ob/default.cfm>. (Accessed February 25, 2021)

The FDA reaffirmed its position in January 2015 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 March 26, 2020)

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## Policy History/Revision Information

Date	Summary of Changes
07/01/2021	<ul style="list-style-type: none"><li>New Medical Policy</li></ul>

## Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage. 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 InterQual<sup>®</sup> criteria, to assist us in administering health benefits. The 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.