Chelation Therapy

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➲ Instructions for Use

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Application

UnitedHealthcare Commercial

This Medical Policy applies to UnitedHealthcare Commercial benefit plans.

UnitedHealthcare Individual Exchange

This Medical Policy applies to Individual Exchange benefit plans.

Coverage Rationale

Chelation for heavy metal toxicity and overload conditions (e.g., iron, copper, lead, aluminum) is proven and medically necessary.

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

- Chelation therapy for treating any chronic, progressive diseases associated with nonoverload 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 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 guidelines may apply.

HCPCS Code	Description
J0470	Injection, dimercaprol, per 100 mg
J0600	Injection, edetate calcium disodium, up to 1,000 mg
J0895	Injection, deferoxamine mesylate, 500 mg
J3490	Unclassified drugs
J3520	Edetate disodium, per 150 mg
J8499	Prescription drug, oral, nonchemotherapeutic, NOS

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

Nonoverload Conditions

Chelation therapy has been proposed as a treatment for various nonoverloaded conditions in which 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 nonoverload conditions has yet to be fully understood. Chelation has been investigated as a treatment for numerous nonoverload conditions, including but not limited to cardiovascular disease, rheumatoid arthritis, 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

Chelation Therapy for Heavy Metal Toxicity and Overload Conditions (e.g., Iron, Copper, Lead, Aluminum)

James and Prakash (2025) conducted a single-center, prospective observational study to assess the efficacy and tolerability of iron chelation with combination deferasirox (DFX) and deferiprone (DFP) in children with transfusion-dependent β-thalassemia major. The study included 27 children (mean age, 8.5 years) who were transfusion dependent and had serum ferritin levels persistently over 2,500 ug/dL for over 6 months while on the maximum dose of DFX (40 mg/kg/day). All participants had DFP added to their ongoing treatment with DFX at the maximum dosage. Serum ferritin levels were monitored at 6-month intervals, and participants were monitored for toxicity for DFP (arthralgia/arthritis and cytopenias) and for DFX (renal function and transaminases), while intolerance to DFX in the form of gastrointestinal symptoms of vomiting/abdominal pain was monitored. Treatment adherence was confirmed by requesting parents to carry the blister packs during assessments. Baseline serum ferritin levels were 4,277 ±1,885 µg/dL (median, 4,241 µg/dL). The authors reported that the mean serum ferritin level decreased significantly to 3,242 ±1,110 µg/dL at 6 months (95% CI, 2,834-3,650 µg/dL; p = 0.003; median, 3,081 µg/dL) and to 2,985 ±1,116 µg/dL at 12 months (95% CI, 2,566-3,404 µg/dL; p = 0.018; median, 2,750 µg/dL) when the participants were on the combination chelation therapy of DFP and DFX. The authors also reported that none of the children needed to stop either DFP or DFX due to bone marrow suppression, hepatic failure, renal dysfunction arthralgia, or arthritis. The authors concluded that combination chelation with DFP and DFX can be considered a viable option for children with transfusion-dependent β-thalassemia major who do not respond to the maximum dose of DFX alone, particularly in resource-limited, rural, and developing settings in which access to intensive chelation therapies may be restricted. Limitations of the study noted by the authors include the inaccessibility of cardiac T2* magnetic resonance imaging (MRI) due to the high cost for most of the participants; observational study design; and lack of a control group. Other limitations include the single-center design and small sample size.

Wilar et al. (2025) conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) to evaluate the efficacy and safety of DFP for the treatment of thalassemia compared (alone or in combination) with those of DFX, deferoxamine (DFO), placebo, or no chelation. All included RCTs focused on children and adults diagnosed with varied thalassemia subtypes who required iron chelation therapy (ICT). The studies also varied in sample sizes, DFP regimens, comparator types, treatment durations, and outcomes reported. Studies that were nonrandomized, were without

comparators, or lacked sufficient data were excluded. The systematic review included 23 RCTs (n = 1,005; mean ages ranged from 2.83-41.3 years), and the meta-analysis included 18 of the RCTs, as five studies were excluded due to insufficient data. The key outcomes assessed across the studies included serum ferritin, liver iron concentration (LIC), urinary iron excretion, cardiac T2* MRI, left ventricular ejection fraction, left ventricular shortening fraction, right ventricular ejection fraction, adverse events (AEs), and all-cause mortality. Various DFP dosing strategies were used in the studies, and the duration of treatment with DFP ranged from 6 to 60 months. The authors reported that DFP significantly improved left ventricular ejection fraction and shortening fraction; however, nonsignificant improvements were observed in urinary iron excretion and right ventricular ejection fraction, and no significant effects were found for serum ferritin, LIC, or cardiac T2* MRI. The authors also reported that (1) DFP increased the risk of AEs but not mortality and that (2) the evidence certainty was moderate for cardiac function and AEs and low for other outcomes. The authors concluded that DFP improves cardiac function and iron excretion, with an acceptable safety profile in thalassemia. They recommended future high-quality RCTs to confirm its role and to optimize regimens. Limitations of this systematic review and meta-analysis include the small sample sizes for some outcomes, which limited the power of the pooled analyses; the number of studies per outcome for some outcomes, which was insufficient for some outcomes to fully assess reporting bias; and the variable risk of bias across studies. Another limitation noted by the authors is the heterogeneity in chelation protocols, comparator arms, and reporting practices, which limited the generalizability of the findings.

Through a systematic review, Lee et al. (2024) explored ICT adherence and the relationship between adherence with health outcomes and health-related quality of life (HRQOL) among individuals with thalassemia. Of 4,917 studies, 20 publications were included. The ICT adherence rate ranged from 20.93% to 75.3%. It also varied per agent, ranging from 48.84% to 85.1% for DFO, 87.2% to 92.2% for DFP, and 90% to 100% for DFX. The majority of studies [n = 10/11 (90.91%)] demonstrated a significantly negative correlation between adherence and serum ferritin, while numerous studies revealed poor ICT adherence linked with an increased risk of liver disease [n = 4/7 (57.14%)] and cardiac disease [n = 6/8 (75%)], endocrinologic morbidity [n = 4/5 (90%)], and lower HRQOL [n = 4/6 (66.67%)]. The limitations of the review include multiple confounding factors, such as the age and sex of individuals as well as the frequency of blood transfusions, which may contribute to variations in the level of adherence. The authors concluded that consistent with expectations, the review demonstrated that adherence to iron chelators maximizes the benefits of the therapy in reducing serum ferritin, iron overload complications, and HRQOL. To fully understand the influence of adherence on the most vulnerable groups, more comprehensive research, with larger sample sizes and assessment of the impact of ICT on the outcomes of interest among different age groups, is required.

In 2023, Salem et al. systematically reviewed the literature to assess the evidence regarding combined DFP and DFX outcomes in individuals with iron overload. The studies included dual iron chelation strategies for several diagnoses. Single-arm studies (n = 7) showed a reduction of serum ferritin, which reached statistical significance in three studies. Likewise, after chelating therapy, most studies reported a numerical decrease in LIC and increased T2* MRI values. Alternatively, comparative studies showed no significant difference in posttreatment serum ferritin between DFX plus DFP and DFX/DFP plus DFO. The adherence to combination therapy was good to average in nearly 66.7% to 100% of the individuals across four studies. One study reported a poor adherence rate. The combined regimen was generally tolerable, with no reported incidence of serious AEs among the included studies. The limitations of the study include the small sample sizes, poor quality of the included studies, limited generalizability, inadequately reported safety outcomes, and lack of newer formulations of DFX and DFP, which is an area of future research. The authors concluded that the DFP and DFX combination is a safe and feasible option for individuals with iron overload and a limited response to monotherapy. Those with severe iron overload had a significant reduction in serum ferritin and LIC and a significant increase in cardiac T2* values after the combined regimen. The combined regimen had a high adherence rate and a well-tolerated safety profile.

Through a randomized, open-label noninferiority study (2022), Kwiatkowski et al. assessed the efficacy and safety of DFP in those participants with sickle cell disease (SCD) or other anemias who were receiving chronic transfusion therapy. Overall, 228 participants were randomized to receive either oral DFP (n = 152) or subcutaneous DFO (n = 76). The primary end point was changed from baseline at 12 months in LIC, assessed by R2* MRI. Noninferiority of DFP was also shown for both cardiac T2* MRI and serum ferritin. The rates of overall AEs, treatment-related AEs, serious AEs, and AEs leading to withdrawal did not differ significantly between the groups. AEs related to DFP treatment included abdominal pain (17.1%), vomiting (14.5%), pyrexia (9.2%), increased alanine transferase (9.2%) and aspartate transferase levels (9.2%), neutropenia (2.6%), and agranulocytosis (0.7%). The study's limitations are related to both agents. For example, DFO must be administered parenterally over 8 to 12 hours per day, which imposes a significant treatment burden for individuals and their caregivers and can impede adherence. DFX is taken orally as tablets or granules, which provides convenience; however, the drug has been associated with hepatic, gastrointestinal, and renal toxicities, which are of particular concern for those with SCD who may have preexisting renal impairment. The authors concluded that the efficacy and safety profiles of DFP were acceptable and consistent with those seen in individuals with transfusion-dependent β-thalassemia.

In 2022, Yang et al. conducted a systematic review and meta-analysis to analyze further ICT's therapeutic potential in lower-risk individuals with myelodysplastic syndrome (MDS). The primary outcome was survival, which was reported as median overall survival or adjusted hazard ratio between the ICT and non-ICT groups. The secondary outcomes included MDS progression rate, acute myeloid leukemia (AML) progression rate, and incidence of cardiac injury. The exploration results demonstrated that the median overall survival in individuals receiving ICT was consistently longer than that in the non-ICT group across the nine studies reporting it. The meta-analysis of observational studies showed that ICT was associated with a lower mortality risk. Five studies indicated a decreased risk, while two indicated an increased risk of AML progression with ICT. Two studies showed a smaller percentage of deaths caused by AML progression, while three studies showed a larger percentage with ICT. In five studies, ICT decreased the risk of cardiac injury. Overall, the study demonstrated that the ICT results provide mortality benefits in those with iron overload and low- or intermediate-risk MDS, in addition to other suggested benefits, including a decreased rate of AML progression and organ dysfunction. However, this observation should be balanced against the cost, complexity, and complications of ICT and the authors' inability to discern the relative efficacy of different types of ICT (DFO, DFP, and DFX) on clinically important outcomes. Based on the available literature, the authors suggested that ICT should be considered in those with low- and intermediate-risk MDS.

In a 2020 multicenter, randomized, double-blinded, placebo-controlled trial (TELESTO), Angelucci et al. evaluated the event-free survival (EFS) and safety of ICT in participants with low- to intermediate-1-risk MDS. The primary end point was EFS, defined as the time from the date of randomization to the first documented nonfatal event (related to cardiac or liver dysfunction and transformation to AML) or death, whichever occurred first. The trial results demonstrated that the median time on treatment was 1.6 years in the DFX group and 1.0 years in the placebo group. Median EFS was prolonged by approximately 1 year with DFX vs placebo. It was reported that AEs occurred in 97.3% of DFX recipients and 90.8% of placebo recipients. Exposure-adjusted incidence rates of AEs in the DFX group vs placebo recipients, respectively, were 24.7 vs 23.9 for diarrhea, 21.8 vs 18.7 for pyrexia, 16.7 vs 22.7 for upper respiratory tract infection, and 15.9 vs 0.9 for increased serum creatinine concentration. The limitations of the trial include the protocol being amended from a phase 3 to a phase 2 study, with a reduced target sample size from 630 to 210 participants. There was differential follow-up between treatment groups. The authors concluded that the findings support ICT in iron-overloaded people with low- to intermediate-1-risk MDS, with longer EFS than placebo and a clinically manageable safety profile. Therefore, ICT may be considered in these individuals.

Maggio et al. (2020) conducted a multicenter, randomized, open-label, noninferiority, phase 3 trial to show the noninferiority of DFP vs that of DFX. Participants were randomly assigned 1:1 to receive orally administered, daily DFP or DFX administered as dispersible tablets, with dose adjustment for 12 months, stratified by age (< 10 years and ≥ 10 years) and balanced by country. The primary efficacy end point was based on predefined success criteria for changes in serum ferritin concentration and cardiac T2* MRI to show the noninferiority of DFP vs that of DFX in the per-protocol population, defined as all randomly assigned participants who received the study drugs and had available data for both variables at baseline and after 1 year of treatment, without significant protocol violations. Noninferiority was based on the two-sided 95% CI of the difference in the proportion of those with treatment success between the two groups and was shown if the lower limit of the two-sided 95% CI was greater than -12.5%. Safety was assessed in all participants who received at least one dose of the study drug. In total, 435 participants were enrolled, with 194 in the DFP group and 199 in the DFX group; 352 of 390 participants had β-thalassemia major, 27 had SCD, five had Thalasso-drepanocytosis, and six had other hemoglobinopathies. The median follow-up was 379 days with DFP and 381 days with DFX. The noninferiority of DFP vs DFX was established [treatment success in 69 of 125 people (55.2%) assigned DFP with primary composite efficacy end point data available at baseline and 1 year vs 80 of 146 (54.8%) assigned DFX; difference, 0.4%; 95% CI -11.9 to 12.6]. No significant difference between the groups was shown in the occurrence of serious and drug-related AEs. The limitations of the study are a low number of participants; the duration of the study, which was less than 1 year; problems with randomization; and different methods used for liver and cardiac MRI assessments. The results showed that in pediatric participants with transfusion-dependent hemoglobinopathies, DFP was effective and safe in inducing control of iron overload during 12 months of treatment. More chelation treatments are needed in pediatric populations, and DFP offers a valuable treatment option for this age group. The authors concluded that the trial supports the use of DFP in pediatric individuals with transfusion-dependent hemoglobinopathies, based on data from the largest randomized clinical trial of ICT in these individuals. The main clinical implication of this study is that pediatric individuals might now have more than one efficacious and safe option for oral ICT.

Hayes (2003; updated 2008) published a Health Technology Assessment that concluded that the use of chelation therapy for overload conditions showed some proven benefit for the treatment of chronic iron overload in individuals with transfusion-dependent anemias and for the treatment of lead overload in children with blood lead levels of over 45 µg/dL; however, the use of chelation therapy for the treatment of aluminum toxicity in individuals undergoing renal dialysis was determined to be of potential but unproven benefit. For children with blood lead levels of less than or equal to 45 µg/dL, Hayes determined that there was insufficient evidence from clinical trials to support the use of chelation therapy.

Chelation Therapy for Nonoverload Conditions

Well-designed, published, and peer-reviewed studies do not support chelation treatment for chronic, progressive diseases such as cardiovascular disease (CVD), atherosclerosis, diabetes, cancer, Alzheimer disease (AD), autism spectrum disorder (ASD), and Parkinson disease (PD). No quality, peer-reviewed studies were identified regarding chelation therapy for the treatment of rheumatoid arthritis, apoplectic coma, chronic fatigue syndrome, chronic renal insufficiency, defective hearing, diabetic ulcer, cholelithiasis, gout, erectile dysfunction, multiple sclerosis, osteoarthritis, osteoporosis, Raynaud disease, renal calculus, schizophrenia, scleroderma, snake venom poisoning, varicose veins, or vision disorders. There is insufficient evidence that chelation therapy is safe and effective for the removal of undesirable metabolites or toxins and that it positively impacts clinical outcomes for different disease states.

Chelation therapy for nonoverload conditions was explored through a Health Technology Assessment performed in 2004 and updated in 2008 by Hayes. The findings were that most studies evaluating chelation therapy for nonoverload were small and flawed by several methodological issues, including heterogeneous populations, nonstandard treatment regimens, insufficient follow-up, subjective outcome measures, and lack of controls or adequate blinding. The report concluded that the available studies evaluating chelation therapy for nonoverload conditions were generally weak, with conflicting findings. The strongest evidence of benefit is for dexrazoxane as a cardioprotective agent in women who are undergoing anthracycline therapy for breast cancer. However, additional studies that include longer follow-ups are needed to confirm this finding and evaluate dexrazoxane's impact on survival. The evidence regarding the effect of chelation therapy on other nonoverload conditions is either conflicting or insufficient and does not support any conclusions regarding efficacy or clinical benefit.

Alzheimer Disease

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 with increased disease occurrence. Some scientists have suggested that chelation therapy may promote beneficial results for individuals with AD by inhibiting the deposition of aluminum in the brain and/or preventing iron from catalyzing the formation of toxic hydroxyl radicals. Aluminum chelators may also reactivate aluminized metalloenzyme complexes in individuals with AD and permit aluminum redistribution in the brain.

Ayton et al. (2025) conducted a phase 2, multicenter, double-masked, placebo-controlled RCT to investigate whether DFP slowed cognitive decline in participants with AD. The study included 81 participants who were over 54 years of age with amyloid-confirmed mild cognitive impairment or early AD. Participants were randomly assigned 2:1 and masked to participants and all study staff. The treatment group (n = 53; mean age, 73.0 years; 54.7% male) received DFP 15 mg/kg twice a day, while the control group (n = 28; mean age, 71.6 years; 60.7% male) received a placebo for 12 months. There were 54 participants who completed the study, with seven (25%) from the control group who withdrew and 20 (37.7%) from the treatment group who withdrew. The primary outcome was a composite cognitive measure obtained at baseline, 6 months, and 12 months using a neuropsychological test battery (NTB) of memory, executive function, and attention tasks. The authors reported that those who received DFP had decreased brain iron accumulation [change in hippocampal quantitative susceptibility mapping for DFP: -0.36 parts per billion (ppb), 95% CI, -0.76 to 0.04 ppb; for placebo: 0.32 ppb, 95% CI, -0.12 to 0.75 ppb] but accelerated cognitive deterioration (change in NTB composite z score for DFP: -0.80, 95% CI, -0.98 to -0.62; for placebo: -0.30, 95% CI, -0.54 to -0.06). The authors also reported that an exploratory analysis of frontal brain regions revealed increased volume loss with DFP, which was consistent with cognitive findings. The authors concluded that these findings suggest that lowering iron with DFP was detrimental in AD. Limitations of this study include the hypothesis that DFP would benefit participants with AD; high dropout rate; high rate of neutropenia (7.5%); impact of the COVID-19 pandemic on recruitment; lack of collection of demographic data on cultural and linguistic backgrounds; and limited follow-up of 12 months.

Sampson et al. (2014) conducted a Cochrane systematic review to evaluate the efficacy of metal protein attenuating compounds for treating cognitive impairment due to AD. The primary outcome measure was cognitive function (measured by psychometric tests). Two metal protein attenuating compound trials were identified. One trial compared clioquinol (PBT1) with a placebo in 36 individuals, with 32 having sufficient data for protocol analysis. There was no statistically significant difference in cognition [as measured on the ADAS-Cog (Alzheimer Disease Assessment Scale-Cognitive)] between the active treatment and placebo groups at 36 weeks, and there was no significant impact on noncognitive symptoms or clinical global impression. In the second trial, a successor compound, PBT2, was compared with a placebo in 78 individuals with mild AD. There was no significant difference in the NTB composite or memory between placebo and PBT2 at week 12. However, two executive function component tests of the NTB showed significant improvement over the placebo in the PBT2 250-mg group from baseline to week 12. There was no significant effect on cognition on the Mini-Mental State Examination or ADAS-Cog scales. PBT2 did have a favorable safety profile. The authors concluded that evidence is absent as to whether clioquinol (PBT1) is safe or has any positive clinical benefit in individuals with AD and

cited that further development of PBT1 has been abandoned. The second trial of PBT2 was more rigorously conducted, and PBT2 appeared to be safe and well tolerated in individuals with mild AD after 12 weeks. Larger trials are now required to demonstrate cognitive efficacy.

Several studies have suggested improving cognitive function or biomarkers in individuals treated with clioquinol or DFO (Crapper Mclachlan et al., 1991; Regland et al., 2001; Ritchie et al., 2003). However, these studies were small, only two were placebo controlled, and none were double blinded; therefore, no conclusions regarding the clinical efficacy of chelation therapy for AD can be made based on these studies.

Autism Spectrum Disorder

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, seventy-seven children with ASD were randomly assigned to receive 7 days of glutathione lotion or placebo lotion, followed by 3 days of oral dimercaptosuccinic acid (DMSA). A total of 49 children who were found to be high excreters of heavy metals during phase 1 continued to phase 2 and received 3 days of oral DMSA or a 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 excreters of heavy metals and received a 3-day course of oral DMSA. Overall, no evidence suggests that multiple rounds of oral DMSA influenced ASD symptoms. The authors concluded that given prior reports of serious AEs such as hypocalcemia, renal impairment, and reported death, the risks of using chelation for ASD currently outweigh the 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 individuals are imperative before further trials are conducted (James et al., 2015).

Cardiovascular Disease

Chelation therapy has been proposed to treat coronary artery disease (CAD), based partly on the hypothesis that chelation could remove atherosclerotic calcium deposits or provide an antioxidant benefit.

Ujueta et al. (2025) conducted a multicenter, double-masked, two-by-two RCT (described below by Lamas et al., 2022; TACT2 trial) to evaluate the efficacy of oral multivitamins and multiminerals (OMVMs), with or without edetate disodium (EDTA)–based chelation, in reducing major adverse cardiovascular events in participants with diabetes and prior myocardial infarction (MI). This study reported the OMVM vs placebo comparison as well as the factorial comparisons. The eligibility requirements included age 50 years or older with a history of an MI at least 6 weeks prior to enrollment. The exclusion criteria included women with childbearing potential; serum creatinine levels of greater than 2.0 mg/dL; a platelet count of less than $100\times10^3/\mu L$; abnormal liver function studies; blood pressure of greater than 160/100 mm Hg; past intolerance of any study component; more than one dose of intravenous chelation therapy or other U.S. Food and Drug Administration–approved chelation drug within 5 years; prior participation in the original TACT; coronary or carotid revascularization planned or having taken place within 6 months; cigarette smoking within 3 months; active heart failure or heart failure hospitalization within 6 months; or inability to tolerate 500-mL infusions weekly. The study included 1,000 participants (median age, 67 years; 73% male) who had a qualifying MI (median of 5 years before enrollment), were diagnosed with diabetes (median time from diagnosis of 14 years; 96% had type 2 diabetes, with 47% requiring insulin), and were randomized 1:1:1:1 into four factorial groups. Group 1 (n = 250) received active OMVM with active intravenous chelation infusions, group 2 (n = 249) received placebo OMVM with active intravenous chelation infusions, group 3 (n = 251) received active OMVM with placebo intravenous infusions, and group 4 (n = 250) received placebo OMVM and placebo intravenous infusions. The authors reported that in participants with chronic coronary disease, diabetes, and a previous MI, the use of OMVM caplets was safe but did not reduce cardiovascular events during a 48-month median follow-up period and that these results are consistent with the much larger body of trial-based evidence that shows no benefit of OMVM for primary prevention. According to the authors, the active OMVM group had a nominally higher proportion of strokes, MI, and death from cardiovascular causes than the placebo OMVM group, but the effect was described as indeterminate due to insufficient precision. The authors stated that they could not replicate the findings from the original TACT trial that showed that the combination of active EDTA chelation and active OMVM significantly reduced the composite primary event rate relative to placebo EDTA/placebo OMVM. The authors concluded that for participants with chronic coronary disease, diabetes, and a previous MI, the use of high-dose OMVMs, alone or in conjunction with EDTA-based chelation, did not reduce cardiovascular events. Limitations noted in the study include that the study was conducted during the COVID-19 pandemic, which may have altered participants' dietary consumption and lifestyle (although all groups would have been affected equally); OMVM adherence was imperfect, with similar discontinuation noted in both the active OMVM and placebo OMVM groups; the TACT2 study was not sufficiently large to detect or rule out an effect size with precision; and questions were raised about OMVM absorption due to the absence of a detectable difference in some minerals in active OMVM vs placebo.

In 2024, Lamas et al. conducted a double-masked, placebo-controlled, multicenter trial at 88 sites of EDTA-based chelation in participants with a previous MI and diabetes. Participants in the trial were aged 50 years or older, had diabetes, and experienced an MI at least 6 weeks before recruitment. The eligible participants were randomly assigned to 40 weekly infusions of an EDTA-based chelation solution or matching placebo and to twice-daily, oral, high-dose multivitamin and mineral supplements or matching placebo for 60 months. The authors compared the effect of EDTA-based chelation and placebo infusion on CVD events and the impact of high doses of oral multivitamins and minerals with oral placebo. The main end point sought was the composite of all causes of mortality, MI, stroke, coronary revascularization, and hospitalization for unstable angina. The median follow-up was 48 months. The primary comparisons were made from participants who received at least one assigned infusion. The trial results demonstrated that of the 959 participants (27% female; 78% White, 10% Black, and 20% Hispanic), 483 received at least one chelation infusion, and 476 received at least one placebo infusion. A primary end point event occurred in 172 participants (35.6%) in the chelation group and 170 (35.7%) in the placebo group. The 5-year primary event cumulative incidence rates were 45.8% in the chelation group and 46.5% in the placebo group. Cardiovascular death, MI, or stroke events occurred in 89 participants (18.4%) in the chelation group and 94 (19.7%) in the placebo group. Death from any cause occurred in 84 participants (17.4%) in the chelation group and 84 (17.6%) in the placebo group. Chelation reduced median blood lead levels from 9.03 µg/L at baseline to 3.46 µg/L at infusion 40 ($p < 0.001$). Corresponding levels in the placebo group were 9.3 µg/L and 8.7 µg/L, respectively. The limitations of the trial include the primary analyses being restricted to a modified intention-to-treat population and treatment adherence being imperfect; additionally, 122 participants were lost to follow-up or withdrew consent, and the therapeutic target of EDTA, which was population levels of blood lead, decreased between the initial study and the present study, possibly reducing the therapeutic efficacy of EDTA. The authors concluded that despite effectively decreasing blood lead levels, EDTA chelation was not effective in reducing cardiovascular events in stable participants with CAD who had diabetes and a history of MI.

In 2022, Lamas et al. conducted a trial to assess the rationale and design of chelation therapy 2 (TACT2) through a randomized, two-by-two factorial, double-masked, placebo-controlled, multicenter clinical trial testing 40 weekly infusions of a multicomponent EDTA [disodium ethylene diamine tetra-acetic acid (EDTA) or Na2EDTA]–based chelation solution and twice-daily, oral, high-dose multivitamin and mineral supplements in those with diabetes and a prior MI. The participants from TACT2 were followed up for 2.5 to 5 years. The primary end point assessed was the composite of the time to first occurrence of all-cause mortality, MI, stroke, coronary revascularization, or hospitalization for unstable angina. One perceived weakness of the initial TACT, when presented in 2012 and published in 2013, was the virtual absence of any underlying accepted hypothesis presented to support the unexpectedly positive results of the trial. The authors concluded that TACT2 may provide definitive evidence of the benefit of EDTA-based chelation on cardiovascular outcomes as well as the clinical importance of longitudinal changes in toxic metal levels in participants.

In 2022, Ravalli et al. systematically reviewed literature related to chelation therapy in individuals with CVD to examine the effect of repeated EDTA on clinical outcomes. Of the 24 studies investigated, predetermined outcomes such as mortality, disease severity, plasma biomarkers of disease chronicity, and quality of life in individuals with preexistent CVD who used EDTA chelation treatments were included. In total, 17 studies, including one RCT, found improvement in individuals' outcomes following EDTA treatment. The most significant improvement was uncovered in the studies that included individuals with a high prevalence of diabetes and/or severe occlusive artery disease. The meta-analysis conducted demonstrated a gain of 0.08 (95% CI, 0.06-0.09) from baseline from four studies reporting the ankle-brachial index. Limitations in the available studies include the small number of RCTs, lack of reported clinical outcomes in several studies, differing infusion regimens, small sample sizes, and limited follow-up data. The authors concluded that this present systematic review of past studies suggests a signal of benefit in individuals with atherosclerotic disease, particularly those with diabetes. Future clinical research on EDTA chelation for individuals with diabetes and peripheral artery disease must include a mechanical component that could clarify if chelation therapy signifies a benefit for this population subgroup, which would contribute to precision environmental medicine. (Lamas et al., 2013, and Knudtson et al., 2002, are included in this systematic review.)

In additional analyses of the TACT study, in 2020, Lewis et al. examined the effect of EDTA chelation therapy as a function of MI location and diabetes. Chelation therapy was associated with a lower risk of the primary end point in 674 individuals post MI (hazard ratio, 0.63; 95% CI, 0.47-0.86; $p = 0.003$) for those with anterior MI. Among individuals post nonanterior MI, totaling 1,034 individuals, chelation therapy was not associated with a lower risk of the primary end points (hazard ratio, 0.96; 95% CI, 0.77-1.20; $p = 0.702$) (p for interaction = 0.032). However, the point estimates of each part of the primary end point favored chelation therapy. The differing treatment effect in individuals with postanterior vs nonanterior MI was consistent among those with or without diabetes and remained significant after adjusting other prognostic variables ($p < 0.01$). There were several limitations to this analysis. First, the individuals with anterior MI had a lower overall event rate than those with nonanterior MI and no difference in the distribution of congestive heart failure or revascularization at baseline. The anterior MI cohort also included significant differences compared with the nonanterior MI cohort, including higher high-density lipoprotein concentrations, lower blood pressure, and lower rates of former

smokers, which may have contributed to the results. There were no quantities of metals or coronary artery calcium at baseline or throughout follow-up to allow mechanistic assessments of the influence of EDTA infusions and for the association of the degree of responsiveness to the results reached. The authors concluded that EDTA-based infusions, compared with placebo, independently reduced the risk of adverse cardiovascular events among stable individuals with prior anterior MI. However, the authors stated that the current results must be considered exploratory and hypothesis generating. These post hoc findings should be taken with caution, and studies specific to individuals with anterior MI should be conducted to confirm these findings.

A Cochrane systematic review of evidence published initially in 2002 was completed by Villarruz-Sulit et al. (2020) to assess the effects of EDTA chelation therapy vs those of placebo or no treatment on clinical outcomes in people with atherosclerotic CVD. The review included five RCTs of EDTA chelation therapy vs placebo or no treatment, with 1,993 randomized individuals. The number of individuals in each study varied widely (from 10 to 1,708 individuals), but all studies compared EDTA chelation with a placebo. The risk of bias for the included studies was generally moderate to low, but one had a high risk of bias because the study investigators broke their randomization code halfway through the study and rolled the placebo individuals over to active treatment. The main outcome measures included all-cause or cause-specific mortality, nonfatal cardiovascular events, direct or indirect measurement of disease severity, and subjective measures of improvement or AEs. Two studies in individuals with CAD reported no evidence of a significant difference in all-cause mortality between chelation therapy and placebo [risk ratio (RR), 0.97; 95% CI, 0.73-1.28; 1,792 individuals; low certainty]. One study in individuals with CAD reported no evidence of a significant difference in coronary heart disease deaths between chelation therapy and placebo (RR, 1.02; 95% CI, 0.70-1.48; 1,708 individuals; very low certainty). Two studies in individuals with CAD reported no evidence of a significant difference in MI (RR, 0.81; 95% CI, 0.57-1.14; 1,792 individuals; moderate certainty), angina (RR, 0.95; 95% CI, 0.55-1.67; 1,792 individuals; very low certainty), or coronary revascularization (RR, 0.46; 95% CI, 0.07-3.25; 1,792 individuals). Two studies [one of the individuals with CAD and one of the individuals with peripheral vascular disease (PVD)] reported no evidence of a significant difference in stroke (RR, 0.88; 95% CI, 0.40-1.92; 1,867 individuals; low certainty). The ankle-brachial pressure index (also known as ankle-brachial index) was measured in three studies, all including individuals with PVD; two studies found no evidence of a significant difference in the treatment groups after 3 months of treatment (mean difference, 0.02; 95% CI, 0.03-0.06; 181 individuals; low certainty). A third study reported an improvement in the ankle-brachial pressure index in the EDTA chelation group, but this study was at an elevated risk of bias. A meta-analysis of maximum and pain-free walking distances 3 months after treatment included individuals with PVD and showed no evidence of a significant difference between the treatment groups (mean difference, -31.46; 95% CI, -87.63 to 24.71; 165 individuals; two studies; low certainty). Quality-of-life outcomes were reported by two studies that included individuals with CAD; however, the authors were unable to pool the data due to different methods of reporting and varied criteria. No major differences between the treatment groups were reported, and none of the included studies reported on vascular deaths. Overall, there was no evidence of major or minor AEs associated with EDTA chelation treatment. The authors concluded that there is currently insufficient evidence to determine the effectiveness or ineffectiveness of chelation therapy in improving the clinical outcomes in people with atherosclerotic CVD. The authors stated that while these results should guide further research, there still is insufficient evidence to support the routine use of chelation therapy in individuals post MI. The publication by Knudtson et al. (2002), previously included in this policy, is included in this systematic review.

A study in the Cochrane review by Escolar et al. (2014) used results of the TACT clinical trial to perform an initial subgroup analysis, which showed a greater effect of EDTA treatment among individuals with a self-reported history of diabetes. Further examination of the data for individuals with diabetes demonstrated a 41% overall reduction in the risk of any cardiovascular event; 40% reduction in the risk of cardiovascular mortality, nonfatal stroke, or nonfatal MI; 52% reduction in recurrent heart attacks; and 43% reduction in death from any cause. In contrast, EDTA treatment showed no significant benefit in the subgroup of 1,045 individuals who did not have diabetes. The authors noted that the results of this analysis support the initiation of clinical trials in individuals 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.

The Cochrane review above included a study by Lamas et al. (2012) that described a pivotal clinical trial, TACT, in detail. The use of chelation therapy in lieu of established therapies, lack of adequate prior research to verify its effectiveness and clinical utility, and overall impact of CAD prompted the National Center for Complementary and Alternative Medicine (now known as the National Center for Complementary and Integrative Health) and the National Heart, Lung, and Blood Institute to sponsor this large-scale clinical study. The 5-year study was a multicenter, double-blinded, randomized efficacy trial from 2002 to 2011 to determine whether EDTA chelation therapy and high-dose oral vitamin and mineral therapy offered clinical, quality-of-life, and economic benefits for individuals with a prior MI. The individuals (n = 1,708) 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. Following the infusion phase of the trial,

individuals were contacted quarterly by telephone, had annual clinic visits, and were seen at the end of the trial or at the 5-year follow-up, whichever occurred first.

Chronic Kidney Disease

In 2025, Murillo et al. conducted an open-label randomized study to investigate the impact of iron chelation on telomere length, oxidative stress, and ferritin levels in those undergoing hemodialysis. The study was conducted with a control group of participants undergoing hemodialysis who would receive DFX treatment for iron chelation for 6 months. The results of the study demonstrated that significant differences were observed in serum ferritin levels and thiobarbituric acid reactive substances. Telomere length had a significant increase after chelation. The serum DFX concentration at zero time at 48 hours was maintained within a 2.67 to 23.78 mmol/L range. The authors concluded that iron chelation in individuals undergoing hemodialysis significantly reduces ferritin and thiobarbituric acid reactive substances and increases telomere length. DFX proves to be beneficial for those with iron overload undergoing hemodialysis. The clinical significance of the findings on patient-centered outcomes is unclear.

Parkinson Disease

Devos et al. (2025) conducted two phase 2 multicenter studies to evaluate the safety and efficacy of using DFP to remove iron from the brain to aid in reducing motor disability progression in participants with early-stage PD who were either dopaminergic treated or treatment naive. Participants who participated were male or female, between 18 and 80 years of age, and diagnosed with early-stage PD within the previous 3 years (defined as the absence of motor fluctuations or L-dopa–induced dyskinesia). The double-blinded, randomized, placebo-controlled SKY clinical trial included 140 adults (mean ±SD age, 61.4 ±9.0 years; 67.7% male; 97.7% White) who were stable on dopaminergic therapy. The participants were randomized to one of four dosage cohorts [300 (n = 27), 600 (n = 26), 900 (n = 25), or 1,200 (n = 28) mg twice daily for 9 months] or to a placebo-matching cohort (n = 28). The total duration of the study was 10 months. There were no significant differences between groups in baseline demographics, MDS-UPDRS (Movement Disorder Society-Unified Parkinson's Disease Rating Scale) Part III total or subscale scores, or Montreal Cognitive Assessment scores. The open-label single-arm EMBARK study enrolled 36 participants (average age, 60.7 years; 72.2% male; 94.4% White) who were on stable dopaminergic therapy (n = 27) or were treatment naive (n = 9) and received 15 mg/kg twice daily. In both studies, the primary outcome was the change from baseline to month 9 in motor examination score, as measured by the MDS-UPDRS Part III. In the SKY study, the authors reported that all doses showed the same worsening as the placebo group, except for the 600-mg dose, which was associated with nonsignificant reductions in the MDS-UPDRS Part III least-squares mean between baseline and 9 months. In the EMBARK study, the authors reported that the trial was terminated before reaching the planned enrollment of 40 participants due to difficulties in both enrollment and retention and that the least-squares mean (SE) changes from baseline in the MDS-UPDRS Part III were nonsignificant [-1.6 (1.7)] in the dopaminergic-treated participants and significant [8.3 (3.9)] in treatment-naive participants, with the latter indicating disease worsening. The authors also reported that AEs possibly related to DFP were reported in 35.7% to 88.9% across all DFP groups vs 42.9% with placebo. The authors concluded that both studies indicated that DFP combined with dopaminergic therapy does not provide significant motor function benefit, while the absence of dopaminergic treatment worsened symptoms. Limitations noted in the SKY study include the small number of participants in each of the four DFP-dosed and placebo groups; high dropout rates (range, 20%-40%); lack of blinding of the participants (due to the number of tablets assigned), who did not know if they were receiving DFP or placebo; and the slow progression of PD over a short period of 9 months in the study. In the EMBARK study, limitations include its termination before reaching planned enrollment and lack of blinding and randomization.

Martin-Bastida et al. (2017) performed a randomized, double-blinded, placebo-controlled trial to investigate whether the iron chelator DFP is well tolerated and able to chelate iron from various brain regions and improve PD symptoms. The study included 22 participants (12 male and 10 female; aged 50-75 years) with early-stage PD and a disease duration of less than 5 years. The participants with PD were recruited between April 4, 2012, and March 27, 2013, and randomly selected to receive a placebo or 20 or 30 mg/kg/day of DFP (80 mg/mL DFP solution or excipient matched placebo provided by ApoPharma Inc., Toronto, ON, Canada), which was divided into two daily, oral doses, morning and evening, and administered for 6 months. Participants were evaluated for PD severity, cognitive function, depression rating, and quality of life. Iron concentrations were assessed in the substantia nigra, dentate and caudate nucleus, red nucleus, putamen, and globus pallidus by T2 MRI at baseline and after 3 and 6 months of treatment. DFP therapy was well tolerated and associated with a reduced dentate and caudate nucleus iron content compared with placebo. Reductions in the iron content of the substantia nigra occurred in only three participants, with no changes being detected in the putamen or globus pallidus. Although 30 mg/kg DFP–treated participants had a trend for improvement in MDS-UPDRS scores and quality of life, this did not reach significance. Cognitive function and mood were not adversely affected by DFP therapy. The authors concluded that short-term DFP therapy in individuals with PD is safe and associated with decreased iron-specific brain regions. A small sample size renders these non–statistically significant findings largely inconclusive. The

findings of this study need to be confirmed by more extensive, well-designed studies assessing patient-centered outcomes.

Mercury "Toxicity" From Dental Amalgam Fillings

Dental amalgams (DAs) have been investigated as a cause of increased blood levels of mercury, potentially associated with several diseases and disorders. While no studies were identified that addressed chelation therapy directly for mercury "toxicity" from amalgam fillings, high-quality, indirect evidence supports the lack of such toxicity. RCTs have concluded that mercury amalgams used in dental restorations cause no harm (Shenker et al., 2008; Bellinger et al., 2006; DeRouen et al., 2006).

In a 2020 systematic review, meta-analysis, and trial of sequential analysis of RCTs, Patini et al. aimed to definitively evaluate the possible effects of exposure to mercury in adults and children with or without DA fillings by measuring the mercury concentration in various biological fluids. The primary outcome measure was the mercury concentration in biological fluids (e.g., urine, hair, blood, saliva) to assess their reliability as biomarkers of mercury exposure. The meta-analysis results were concluded from data gathered from 859 individuals, but group differences were not significant ($p = 0.12$). The trial sequential analysis confirmed that the evidence revealed that it was due to the lack of statistical power, since the required information size threshold was not reached. The lack of longer RCTs that assess various types of adverse effects linked to using DA was a limiting factor in the review. The authors concluded that the existing evidence reveals insufficient data to support the hypothesis that restorations with DA can cause nephrotoxicity compared with the composite resins' restorations.

Golding et al. (2016) evaluated the extent to which DA may contribute to total blood mercury (TBHg) levels in pregnant women in a single geographic region in the UK. The authors reviewed the laboratory assay results for total mercury levels in whole blood samples from 4,484 pregnant women and concluded that the number of DA fillings was responsible for at least 6.47% of the individuals' TBHg levels. For perspective, in an earlier publication, the authors noted that 8.75% of the TBHg level was shown to be attributable to seafood consumption in the same study population. The number of amalgams in the individuals' mouths at the start of pregnancy accounted for most of the variance in dental variability. The authors noted that the measures of DA exposure were at risk of recall bias, as they were dependent on the responses to a retrospective questionnaire completed 2 years after the study child's delivery. The questions asked in the questionnaire regarding dental care received before and during the pregnancies were inserted in the middle of the questionnaire, without reference to any outcome to minimize bias. Another disadvantage to the study noted by the authors was that the timing of the blood draw in relation to the timing of any dental work was not known. The authors concluded that DA contributes a comparable amount of variance in TBHg to seafood consumption in this population and that there is no evidence to date that fetal exposures to mercury from maternal DAs cause adverse effects in a developing child.

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; reviewed 2024).

American Academy of Pediatrics (AAP) Council on Environmental Health

As part of the Choosing Wisely initiative, in 2021, the AAP released *Five Things Physicians and Patients Should Question* regarding environmental health and autism. The AAP Council on Environmental Health recommends against ordering chelation challenge urinary analyses for children with suspected lead poisoning. The chelation challenge was formerly used to assess whether a child had a significant body burden of lead or lead poisoning and whether formal chelation would result in significant lead clearance. Evidence suggests that the chelation challenge has no better prognostic value than the standard blood lead level. Further, there is some evidence that the chelation challenge may be potentially dangerous. In summary, the chelation challenge has no clinical utility in treating childhood lead poisoning today (Mackara, 2021).

American College of Cardiology (ACC)/American Heart Association (AHA) Task Force on Practice Guidelines/American Association for Thoracic Surgery (AATS)/Preventive Cardiovascular Nurses Association (PCNA)/Society for Cardiovascular Angiography and Interventions (SCAI)/Society of Thoracic Surgeons (STS)

The ACC/AHA/AATS/PCNA/SCAI/STS concludes 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 CVD. Accordingly, the group finds that the usefulness of chelation therapy in cardiac disease is highly questionable (Fihn et al., 2014).

American College of Medical Toxicology (ACMT)

A position statement released by the ACMT on September 26, 2013, concludes that chelation is not recommended for any condition other than documented metal intoxication that has been diagnosed using validated tests in appropriate biological samples. Chelation does not improve objective outcomes in autism, CVD, or neurodegenerative conditions like AD. Chelating drugs may have significant side effects, including dehydration, hypocalcemia, kidney injury, liver enzyme elevations, hypotension, allergic reactions, and essential mineral deficiencies, even when used for appropriately diagnosed metal intoxication. Inappropriate chelation, which may cost hundreds to thousands of dollars, risks these harms as well as neurodevelopmental toxicity, teratogenicity, and death (released 2013 and 2015; last reviewed 2021).

American College of Physicians (ACP)

The ACP, American College of Cardiology Foundation, AHA, and three other medical associations published joint clinical practice guidelines on managing stable ischemic heart disease. The guidelines recommend that "chelation therapy should not be used to improve symptoms or reduce cardiovascular risk for individuals with stable ischemic heart disease" (Qaseem et al., 2012).

In 2004, the ACP's clinical practice guidelines said that chelation "should not be used to prevent MI or death or to reduce symptoms for individuals with symptomatic chronic stable angina" (Snow et al., 2004).

American Heart Association (AHA)

The *2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for the Management of Patients With Chronic Coronary Disease* offers an update to and combines new evidence since the *2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease* and the corresponding *2014 ACC/AHA/AATS/PCNA/SCAI/STS Focused Update of the Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease*. This guideline provides an evidenced-based and patient-centered approach to the management of patients with chronic coronary disease, considering social determinants of health and incorporating the principles of shared decision-making and team-based care. The guideline states that EDTA is presently not approved by the U.S. Food and Drug Administration for preventing or treating CVD (Virani et al., 2023).

Canadian Cardiovascular Society

The evidence-based consensus guidelines (2014) from the Canadian Cardiovascular Society include 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 (Mancini et al., 2014).

National Institute for Health and Care Excellence (NICE)

A NICE guideline on autism does not recommend using chelation to manage core symptoms of autism in adults (2012; updated 2021).

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 for metal poisoning or iron overload treatment. Use is limited to FDA-approved indications for each chelation agent, as referenced in a generally recognized drug compendium (e.g., American Hospital Formulary Service Drug Information®, DRUGDEX® System). Additional information is available at: http://www.accessdata.fda.gov/scripts/Cder/ob/default.cfm. (Accessed March 3, 2026)

The FDA issued updated recommendations concerning dental amalgam (DA) and potential risks to certain high-risk individuals that may be associated with mercury-containing fillings. In 2020, the FDA released a statement saying that certain groups may be at risk for potential harmful health effects; the agency recommends that certain high-risk groups avoid getting DA when possible and appropriate. These groups that may be at greater risk for potential harmful health effects include:

- Pregnant women and their developing fetuses
- Women who are planning to become pregnant
- Nursing women and their newborns and infants

- Children, especially those younger than 6 years of age
- People with preexisting neurological diseases such as multiple sclerosis, Alzheimer disease, or Parkinson disease
- People with impaired kidney function; and
- People with known heightened sensitivity (allergy) to mercury or other components of DA

Additional information is available at: https://www.fda.gov/news-events/press-announcements/fda-issues-recommendations-certain-high-risk-groups-regarding-mercury-containing-dental-amalgam. (Accessed March 3, 2026)

On their website that addresses health fraud from medications for specific diseases and conditions, the FDA states that unproven drug products for sale that claim to cure or treat autism spectrum disorders are misleading and deceptive, as this condition currently has no cure. Additional information is available at: https://www.fda.gov/drugs/medication-health-fraud/medication-health-fraud-specific-diseases-and-conditions#:~:text=the%20aging%20process.-,Autism%20Medication%20Health%20Fraud,that%20currently%20has%20no%20cure. (Accessed March 3, 2026)

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Policy History/Revision Information

Date	Summary of Changes
07/01/2026	**Supporting Information** • Updated *Clinical Evidence*, *FDA*, and *References* sections to reflect the most current information • Archived previous policy version 2026T0051DD

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, 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.

This Medical Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, 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.