Chelation Therapy for Non-Overload Conditions (for Louisiana Only)

Policy Number: CS016LA.J~~I~~
Effective Date: ~~October 1, 2020~~**TBD**

Instructions for Use

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Application

This Medical Policy only applies to the state of Louisiana.

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~~**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
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 ~~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 **Parkinson's Disease** ~~RA~~. ~~There~~

~~are no~~**No quality peer-reviewed** studies ~~available~~ **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, ~~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 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 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, 2 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 (Crapper**,** 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~~ bas**ed**~~is~~ **on**~~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).~~

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 2 phases. During Phase 1, 77 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 on to Phase 2 and received 3 days of oral DMSA or placebo followed by 11 days off, with the cycle repeated up to 6 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 who received a 3 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 hypocalc~~a~~emia, 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. [FDL1]

An updated Cochrane systematic review of evidence originally published in 2002 was completed by Villarruz-Sulit et al. (2020) to assess the effects of ethylene diamine tetra-acetic acid (EDTA) chelation therapy versus placebo or no treatment on clinical outcomes among people with atherosclerotic cardiovascular disease (ASCVD). The review included 5 studies that were randomized controlled trials of EDTA chelation therapy versus placebo or no treatment, with a total of 1,993 randomized participants. The number of participants in each study varied widely (from 10 to 1708 participants), but all studies compared EDTA chelation to a placebo. Risk of bias for the included studies was generally moderate to low, but one study had high risk of bias because the study investigators broke their randomization code halfway through the study and rolled the placebo participants over to active treatment. The main outcome measures included all-cause or cause-specific mortality, non-fatal cardiovascular events, direct or indirect measurement of disease severity, and subjective measures of improvement or adverse events. Two studies with participants 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 to 1.28; 1792 participants; low certainty). One study with participants 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 to 1.48; 1708 participants; very low certainty). Two studies with participants with CAD reported no evidence of a significant difference in myocardial infarction (RR 0.81, 95% CI 0.57 to 1.14; 1792 participants; moderate certainty), angina (RR 0.95, 95% CI 0.55 to 1.67; 1792 participants; very low certainty), or coronary revascularization (RR 0.46, 95% CI 0.07 to 3.25; 1792 participants). Two studies (one of participants with CAD and one of participants with peripheral vascular disease (PVD)) reported no evidence of a significant difference in stroke (RR 0.88, 95% CI 0.40 to 1.92; 1867 participants; low certainty). Ankle-brachial pressure index (ABPI; also known as ankle brachial index) was measured in three studies, all including participants with PVD; two studies found no evidence of a significant difference in the treatment groups after three months of treatment (mean difference (MD) 0.02, 95% CI-0.03 to 0.06; 181 participants; low-certainty). A third study reported an improvement in ABPI in the EDTA chelation group,

but this study was at high risk of bias. Meta-analysis of maximum and pain-free walking distances three months after treatment included participants with PVD and showed no evidence of a significant difference between the treatment groups (MD-31.46, 95%CI-87.63 to 24.71; 165 participants; 2 studies; low-certainty). Quality of life outcomes were reported by two studies that included participants 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 was reported. None of the included studies reported on vascular deaths. Overall, there was no evidence of major or minor adverse events 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 clinical outcomes of people with ASCVD. More high-quality, randomized controlled trials are needed that assess the effects of chelation therapy on longevity and quality of life among people with ASCVD.

The Cochrane review above included a study by Lamas et al (2012) that described a pivotal clinical trial, the Trial to Assess Chelation Therapy (TACT), in detail. 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 this large-scale clinical study. The 5-year study was a multicenter, double-blind, randomized efficacy trial that took place 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 patients with a prior myocardial infarction. The participants (n=1708) 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, participants 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.

~~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.~~

~~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.~~

Analysis of the data from this TACT study was also included in the updated Cochrane review by Villarruz-Sulit. The study 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 reported that the primary endpoint occurred in 222 (26%) of the chelation group and 261 (30%) of the placebo group indicating that the primary outcome barely reached the pre-specified statistical significance level, and therefore the role of chance in these findings was 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 (Lamas et al 2013).

Another study in the updated 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 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.

The updated Cochrane review (above, by Villarruz-Sulit) also included a randomized controlled trial (RCT) by Knudtson et al. (2002) to determine if chelating agent, EDTA protocols have a favorable impact on exercise ischemia threshold and quality of life measures in patients with stable ischemic heart disease. The study included 84 patients who were randomized between January 1996 and January 2000. Of the 84 patients randomized, 78 completed treatments, the final treadmill test, and the final quality of life assessments (39 in each group). Four placebo patients and 2 chelation patients were unable to complete the treatment phase. Patients were randomly assigned to receive infusion with either weight-adjusted (40 mg/kg) EDTA chelation therapy (n=41) or placebo (n=43) for 3 hours per treatment, twice weekly for 15 weeks and once per month for an additional 3 months. Patients in both groups took oral multivitamin therapy as well. Thirty-nine patients in each group completed the 27-week protocol. One patient undergoing chelation had therapy discontinued for a transient rise in serum creatinine. The mean

(SD) baseline exercise time to ischemia was 572 (172) and 589 (176) seconds in the placebo and chelation groups, respectively. The corresponding mean changes in time to ischemia at 27 weeks were 54 seconds (95% confidence interval [CI], 23-84 seconds; P<.001) and 63 seconds (95% CI, 29-95 seconds; P<.001), for a difference of 9 seconds (95% CI, −36 to 53 seconds; P=.69). Exercise capacity and quality of life scores improved by similar degrees in both groups. The authors concluded Based on exercise time to ischemia, exercise capacity, and quality of life measurements, there is no evidence to support a beneficial effect of chelation therapy in patients with ischemic heart disease, stable angina, and a positive treadmill test for ischemia.

Parkinson's Disease

A randomized double-blinded placebo-controlled trial (RCT) was performed by Martin-Bastida et al. (2017) to investigate whether iron chelator, deferiprone, is well tolerated and able to chelate iron from various brain regions and improve Parkinson's disease (PD) symptomology. The study included 22 patients (12 males and 10 females; aged 50-75 years) with early-stage PD, disease duration of less than five years. The PD patients were recruited between April 4, 2012, and March 27, 2013, and randomly selected to receive placebo or 20 or 30 mg/kg/day deferiprone (80 mg/mL deferiprone solution or excipient matched placebo provided by ApoPharma Inc., Toronto, ON, Canada) which was divided into 2 daily oral doses, morning and evening, and administered for 6 months. Patients were evaluated for PD severity, cognitive function, depression rating and quality of life. Iron concentrations were assessed in the substantia nigra (SNc), dentate and caudate nucleus, red nucleus, putamen and globus pallidus by T2 MRI at baseline and after 3 and 6 months of treatment. Deferiprone therapy was well tolerated and was associated with a reduced dentate and caudate nucleus iron content compared to placebo. Reductions in iron content of the SNc occurred in only 3 patients, with no changes being detected in the putamen or globus pallidus. Although 30 mg/kg deferiprone treated patients showed a trend for improvement in Movement Disorders Society – Unified Parkinson's Disease Rating Scale (MDS-UPDRS) scores and quality of life, this did not reach significance. Cognitive function and mood were not adversely affected by deferiprone therapy. The authors concluded that short term deferiprone therapy in PD patients is safe and associated with decreases in iron specific brain regions. A small sample size renders these non-statistically significant findings largely inconclusive . The findings of this study need to be validated by larger and well-designed studies.

~~*Rheumatoid Arthritis*~~

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

Clinical Practice Guidelines

~~*Professional Societies*~~

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 Medical Toxicology (ACMT)

A position statement released by the American College of Medical Toxicology on September 26, 2013, concluded that chelation is not recommended for any condition other than documented metal intoxication which has been diagnosed using validated tests in appropriate biological samples. Chelation does not improve objective outcomes in autism, cardiovascular disease or neurodegenerative conditions like Alzheimer's disease. Even when used for appropriately diagnosed metal intoxication, chelating drugs may have significant side effects, including dehydration, hypocalcemia, kidney injury, liver enzyme elevations, hypotension, allergic reactions and essential mineral deficiencies. Inappropriate chelation, which may cost hundreds to thousands of dollars, risks these harms, as well as neurodevelopmental toxicity, teratogenicity and death.

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". ~~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).

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).

National Institute for Health and Care Excellence (NICE)

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). [SDNA2]

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 stud~~y~~**ies** w~~as~~**ere** identified that addressed ~~directly~~ chelation **directly** therapy for mercury "toxicity" from amalgam fillings, indirect high-quality evidence supports 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).

Golding et al (2015) evaluated the extent to which dental amalgam (DA) may contribute to total blood mercury (TBHg) levels of 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 of 4,484 pregnant women and concluded that the number of DA fillings is responsible for at least 6.47% of the participants' TBHg level. For perspective, in a previous 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 participants' 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 that was completed two years following the delivery of the study child. 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 on a developing child.

~~***Professional Societies***~~

~~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)

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

~~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.~~

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) ~~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 **February 22, 2022**~~March 26, 2020~~)

The FDA reaffirmed its position in ~~January 2015~~**September 2020** 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: **https://www.fda.gov/medical-devices/safety-communications/recommendations-about-use-dental-amalgam-certain-high-risk-populations-fda-safety-communication.**~~http://www.ada.org/en/press-room/news-releases/2015-archive/january/fda-updates-consumer-advisory.~~
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consent of UHC.~~Voest EE, Vreugdenhil G, Marx JJM. Iron-chelating agents in non-iron overload conditions. Ann Intern Med. 1994;120(6):490-499.~~

Policy History/Revision Information

Date	Summary of Changes
TBD	**Supporting Information** • Updated ***Description of Services, Clinical Evidence, FDA, and References*** sections to reflect the most current information • Archived previous policy version CS016LA.J

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® 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.