BlueCross BlueShield of Alabama

Name of Policy:
Chelation Therapy

Policy #: 085
Category: Pharmacology

Latest Review Date: February 2018
Policy Grade: A

Background/Definitions:

As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. *The technology must have final approval from the appropriate government regulatory bodies;*
2. *The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
3. *The technology must improve the net health outcome;*
4. *The technology must be as beneficial as any established alternatives;*
5. *The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. *In accordance with generally accepted standards of medical practice; and*
2. *Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
3. *Not primarily for the convenience of the patient, physician or other health care provider; and*
4. *Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.*

Description of Procedure or Service:

Chelation therapy is an established treatment for the removal of metal toxins by converting them to a chemically inert form that can be excreted in the urine. Chelation therapy consists of the intravenous or oral administration of chelating agents that remove metal ions such as lead, aluminum, mercury, arsenic, zinc, iron, copper, and calcium from the body. Specific chelating agents are used for particular heavy metal toxicities.

There are a number of indications for chelation therapy that have received FDA approval and for which chelation therapy is considered standard of care treatment. These include:

- Extreme conditions of metal toxicity
- Treatment of chronic iron overload due to blood transfusions and due to non-transfusion dependent thalassemia
- Wilson disease
- Lead poisoning
- Control of ventricular arrhythmias or heart block associated with digitalis toxicity; and
- Emergency treatment of hypercalcemia

Chelation therapy has been investigated for a variety of other applications including treatment of atherosclerosis, arthritis, diabetes, multiple sclerosis, and autism. However, there is insufficient evidence that chelation therapy improves health outcomes for any condition other than those that have received FDA approval.

Another class of chelating agents, called metal protein attenuating compounds (MPACs), is under investigation for the treatment of Alzheimer's disease, which is associated with the disequilibrium of cerebral metals. Unlike traditional systemic chelators that bind and remove metals from tissues systemically, MPACs have subtle effects on metal homeostasis and abnormal metal interactions. In animal models of Alzheimer's disease, they promote the solubilization and clearance of Aβ-amyloid protein by binding its metal-ion complex and also inhibit redox reactions that generate neurotoxic free radicals. MPACs therefore interrupt two putative pathogenic processes of Alzheimer's disease. However, no MPACs have received U.S. Food and Drug Administration (FDA) approval for the treatment of Alzheimer's disease.

Policy:

Chelation therapy meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage in the treatment of **each** of the following conditions **when performed in the in-patient setting**:

- Control of ventricular arrhythmias or heart block associated with digitalis toxicity;
- Emergency treatment of hypercalcemia;
- *Extreme conditions of metal toxicity (i.e. arsenic, cadmium, copper, mercury);
- Treatment of chronic iron overload due to blood transfusions (transfusional hemosiderosis) and due to non-transfusion-dependent thalassemia (NDTD);
- Wilson's disease (hepatolenticular degeneration); **and**
- Lead poisoning.

Chelation therapy for the treatment of sickle cell anemia, thalassemias, and iron overload in patients requiring frequent transfusion meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage when **taken orally, or performed as an outpatient procedure, or given in the home health setting.**

Chelation therapy in any form (IV, PO, transdermal, topical or rectal) **does not meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage when **performed in an inpatient or outpatient setting to treat any other condition**; including but not limited to, Alzheimer's disease, atherosclerosis, myocardial infarction, autism, and diabetes, and is considered **investigational**.

Any treatment associated with non-covered chelation therapy (e.g. glutathione and vitamin C) **does not meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage and is considered **investigational**.

***Chelation therapy performed to treat heavy metal and/or lead poisoning detected by a provocative urine test does not meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage.

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the member's contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

This policy was updated with a literature search through December 11, 2017.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Chelation therapy is an established treatment for the medically necessary indications listed above, particularly for the treatment of metal toxicity and transfusional hemosiderosis. Literature searches have focused on the use of chelation therapy for other conditions including, but not limited to, atherosclerosis, autism, Alzheimer's disease, arthritis, multiple sclerosis and diabetes.

Alzheimer Disease

A 2008 Cochrane Review evaluated metal protein attenuating compounds (MPAC) for treating Alzheimer's disease. The review identified one placebo-controlled RCT. This study, by Richie and colleagues, was published in 2003. Patients were treated patients with PBT1, a MPAC also known as clioquinol, an anti-fungal medication that crosses the blood-brain barrier. Clioquinol was withdrawn for oral use in 1970 because of its association with subacute myelo-optic neuropathy. In the study, oral clioquinol was administered in doses increasing to 375 mg twice daily to 16 Alzheimer's disease patients and the effects were compared to 16 matched controls who received placebo. At 36 weeks, there was no statistically significant between-group difference in cognition measured by the Alzheimer's disease Assessment Scale – Cognitive (ADAS-Cog scale). One patient in the treatment group developed impaired visual acuity and color vision during weeks 31 to 36 while she was receiving clioquinol, 375 mg twice daily. Her symptoms resolved on treatment cessation. A 2012 update of this Cochrane review included trials through December 2011. Only the Lannfelt trial (discussed next) was identified.

Further studies of PBT1 have been abandoned in favor of a successor compound, PBT2. Lannfelt and colleagues (2008) completed a double-blind, placebo-controlled RCT in which 78 Alzheimer's disease patients were treated for 12 weeks with 50 mg PBT2 (n=20), 250 mg PBT2

(n=29), or placebo (n=29). There was no statistically significant difference in ADAS-Cog scale or Mini-Mental Status Exam scores among groups in this short-term study. The most common adverse event was headache. Two serious adverse events (urosepsis and transient ischemic event) were reported, both by patients receiving placebo.

Section Summary: Alzheimer Disease
There is insufficient evidence on the safety and efficacy of chelation therapy for treating patients with Alzheimer disease. The few published RCTs did not find that chelation was superior to placebo for improving health outcomes.

Cardiovascular Disease
Atherosclerosis
In 2002, a Cochrane review was published evaluating studies on EDTA chelation therapy for treating patients with atherosclerotic cardiovascular disease. Five randomized placebo-controlled were identified, none of which reported mortality, non-fatal events and cerebrovascular vascular events. Four of the five studies (total n=250) found no significant benefits of EDTA chelation therapy on outcomes reported including direct or indirect measurement of disease severity and subjective measures of improvement. The fifth study, which included only ten patients, was apparently stopped early due to benefit, but relevant outcome data were not available. The Cochrane reviewers concluded that evidence was insufficient to draw conclusions about the efficacy of chelation therapy for treating atherosclerosis. Additional RCTs that report health outcomes including mortality and cerebrovascular events were suggested.

Among the published RCTs, Knudtson and colleagues (2002) randomized 84 patients with coronary artery disease and a positive treadmill test to receive EDTA chelation therapy or placebo. Treatment was administered for three hours twice weekly for 15 weeks, and once per month for an additional three months. Outcome measures included change in time to ischemia, functional reserve for exercise, and quality of life. There was no significant difference between the two groups. Another double-blind, placebo controlled RCT of EDTA chelation showed no difference between the two groups in short- or long-term improvement in vasomotor response. Two small randomized trials from the 1990s have also reported no benefit of chelation therapy as a treatment of peripheral arterial disease.

Section Summary: Atherosclerosis
Several RCTs published on chelation therapy for treating atherosclerosis generally have reported intermediate outcomes and have not found EDTA chelation therapy to be more effective than placebo. Additional RCTs that report health outcomes are needed to establish the efficacy of this treatment.

Myocardial Infarction (MI)
In 2013, Lamas et al published results of the multicenter, 2x2 factorial, randomized double-blind Trial to Assess Chelation Therapy (TACT). The trial included 1,708 individuals, age 50 or older, who had a history of a myocardial infarction at least six weeks previous and a serum creatinine level of 2.0 mg/dL or less. Patients were randomized to receive 40 infusions of disodium EDTA (n=839) or placebo (n=869). Patients also received either oral high-dose vitamin and mineral therapy or placebo. The first 30 infusions were given weekly, and the remaining ten infusions

were given two to eight weeks apart. The primary endpoint was a composite outcome that included death from any cause, reinfarction, stroke, coronary revascularization or hospitalization for angina at five years. The threshold for statistical significance was adjusted for multiple interim analyses to a p value of 0.036. A total of 361 patients in the chelation group (43%) and 464 patients in the placebo group (57%) discontinued treatment after starting it, withdrew consent during follow-up or were lost to follow-up. The Kaplan-Meier five year estimates for the primary endpoint were 32.8% (95% confidence interval [CI]: 29.1% to 36.5%) in the chelation group and 38.5% (95% CI: 34.6% to 42.3%) in the control group. The difference between groups was statistically significant (p = 0.035). The most common individual clinical endpoint was coronary revascularization, which occurred in 130 of 839 patients (16%) in the chelation group and 157 of 869 patients (18%) in the control group, p value=0.08. The next most frequent endpoint was death. This occurred in 87 of 839 (10%) of patients in the chelation group and 93 of 869 (11%) of patients in the placebo group, p value=0.64. None of the individual components of the primary outcome differed significantly between groups; however, the study was not powered to detect difference in individual components. Four severe adverse events occurred that were definitely or possibly related to study therapy. There were two events each in the treatment and control group, including one death in each group. Quality of life outcomes (reported in 2014) did not differ between groups with two years of follow up.

Another 2014 follow-up publication reported results of the four treatment groups in the 2×2 factorial design (double active group [disodium EDTA infusions with oral high-dose vitamins; n=421 patients randomized], active infusions with placebo vitamins [n=418], placebo infusions with active vitamins [n=432], and double placebo [n=437]). The proportion of patients who discontinued treatment, withdrew consent, or were lost to follow-up per treatment group was not reported. Five-year Kaplan-Meier estimates for the primary composite end point were 32%, 34%, 37%, and 40%, respectively. The reduction in primary end point by double active treatment compared with double placebo was statistically significant (hazard ratio [HR], 0.74 [95% CI, 0.57 to 0.95]). In 633 patients with diabetes (≈36% of each treatment group), the primary end point reduction of double active compared with double placebo was more pronounced (HR=0.49 [95% CI, 0.33 to 0.75]).

The trial was limited by the high number of withdrawals, with differential withdrawals between groups. The primary end point included components of varying clinical significance, and the largest difference between groups was for revascularization events. The primary end point barely met the significance threshold; if more patients had remained in the study and experienced events, results could have differed. Moreover, as noted in an editorial accompanying the original (2013) publication, 60% of patients were enrolled at centers described as complementary and alternative medicine sites, and this may have resulted in a population that is not generalizable to that seen in general clinical care. Editorialists commenting on the subsequent (2014) publication suggested that further research is warranted to replicate the findings. This secondary analysis has the same limitations as the parent study previously described, namely, high and differential withdrawal and heterogeneous composite end point. Additionally, because diabetes was not a stratification factor in TACT, results of this subgroup analysis are preliminary and require replication.

Section Summary: Myocardial Infarction
One RCT with limitations, including high dropout with differential drop-out between groups, reported that cardiovascular events are reduced in patients treated with chelation therapy. This effect was greater among patients with diabetes mellitus. However, this was not a high-quality trial and therefore results may be biased. Further trials that are of high quality are needed to corroborate whether chelation therapy improves outcomes in patients with prior MI.

Autism Spectrum Disorder
Based on similarities between mercury poisoning and autism spectrum disorder symptoms, Bernard and colleagues (2001) hypothesized a link between environmental mercury and autism. This theory was rejected by Nelson and Bauman, who found that many of the characteristics of mercury poisoning such as ataxia, constricted visual fields, peripheral neuropathy, hypertension, skin eruption, and thrombocytopenia, are never seen in autistic children. In 2007, a meta-analysis by Ng and colleagues concluded that there was no association between mercury poisoning and autism.

In 2009, Rossignol published a systematic review of novel and emerging treatments for autism and did not identify any studies that included a control group. The author stated the case series suggested a potential role for chelation in treating some autistic individuals with known elevated heavy metal levels, but this possibility needed further investigation in controlled studies.

Section Summary: Autism Spectrum Disorder
There is a lack of controlled studies on the effect of chelation therapy on health outcomes in patients with autism.

Diabetes
Cardiovascular Disease in Patients with Diabetes
A 2009 trial by Cooper and colleagues in New Zealand evaluated the effect of copper chelation using oral trientine on left-ventricular hypertrophy in 30 patients with type 2 diabetes. A total of 21/30 (70%) of the participants completed the 12-month follow-up. At 12 months, there was a significantly greater reduction in left ventricular mass indexed to body surface area (LVM) in the group receiving active treatment compared to placebo (-10.6 g/m2 vs. -0.1 g/m2, p=0.01). The study was limited by the small sample size and high drop-out rate.

Escolar et al (2014) published results of a prespecified subgroup analysis of diabetic patients in TACT. In TACT, there was a statistically significant interaction between treatment (EDTA or placebo) and presence of diabetes: Among 538 (31% of the trial sample) self-reported diabetic patients, those randomized to EDTA had a 39% reduced risk of the primary composite outcome compared with placebo (HR=0.61; 95% CI, 0.45 to 0.83; p=0.02); among 1170 nondiabetic patients, risk of the primary outcome did not differ statistically between treatment groups (HR=0.96; 95% CI, 0.77 to 1.20; p=0.73). For the subsequent subgroup analysis, the definition of diabetes mellitus was broadened to include self-reported diabetes, use of oral or insulin treatment for diabetes, or fasting blood glucose of 126 mg/dL or more at trial entry. Of 1708 patients in TACT, 633 (37%) had diabetes mellitus by this definition: 322 were randomized to EDTA and 311 to placebo. Compared with all other trial participants, this subgroup of diabetic patients had higher body mass index, fasting blood glucose, and prevalence of heart failure,

stroke, hypertension, peripheral artery disease, and hypercholesterolemia. Within this subgroup, baseline characteristics were similar between treatment groups. With approximately 5 years of follow-up, the primary composite end point occurred in 25% of the EDTA group and 38% of the placebo group (HR=0.59; 99.4% CI, 0.39 to 0.88 [adjusted for multiple subgroups]; p=0.002). In adjusted analysis of the individual components of the primary end point, there were no statistically significant differences between treatment groups. Thirty-six adverse events attributable to study drug that led to trial withdrawal, 16 in the EDTA group and 20 in the placebo group.

Diabetic Nephropathy

Chen et al (2012) conducted a single-blind RCT of chelation therapy effects on the progression of diabetic nephropathy in Chinese patients with high-normal lead levels. Fifty patients with diabetes, high-normal body lead burden (80-6,000 µg), and serum creatinine 3.8 mg/dL or lower were included. Baseline mean blood lead levels were 6.3 µg/dL in the treatment group and 7.1 µg/dL in the control group; baseline mean body lead burden was 151 µg in the treatment group and 142 µg in the control group. According to the U.S. Occupational and Health Safety Administration (OSHA), the maximum acceptable blood lead level in adults is 40 µg/dL. Patients were randomized to three months of calcium disodium EDTA or placebo. During 24 months of treatment follow up, patients in the chelation group received additional chelation treatments as needed (i.e., if serum creatinine level exceeded pre-treatment levels or body lead burden was >60 ug) and patients in the placebo group continued to receive placebo medication. All patients completed the 27-month study. The primary outcome was change in estimated glomerular filtration rate (eGFR). Mean (SD) yearly rate of decrease in eGFR was 5.6 mL/min/173 m2 in the chelation group and 9.2 mL/min/173 m2 (SD: 3.6) in the control group. The difference between groups was statistically significant, p=0.04. The secondary endpoint was the number of patients in whom the baseline serum creatinine doubled or who required renal replacement therapy. A total of nine patients (36%) in the treatment group and 17 (68%) in the control group attainted the secondary endpoint; the difference between groups was statistically significant (p=0.02). There were no reported side effects of chelation therapy during the 27-month study period.

Section Summary: Diabetes

Two small RCTs with limitations represent insufficient evidence that chelation therapy is effective for treating cardiovascular disease in patients with diabetes. One small single-blind RCT is insufficient evidence that chelation therapy is effective for treating diabetic nephropathy in patients with high-normal lead levels. Additional RCTs with larger numbers of patients and that report health outcomes such as cardiovascular events, end-stage renal disease and mortality are needed.

Other Potential Indications

No RCTs or other controlled studies were identified that evaluated the safety and efficacy of chelation therapy for other conditions such as multiple sclerosis or arthritis. Iron chelation therapy is being investigated for Parkinson disease and endotoxemia.

Summary

The evidence for chelation therapy in individuals who have Alzheimer disease, cardiovascular disease, arthritis, autism, arthritis, diabetes, or multiple sclerosis consists of a small number of RCTs and case series. Relevant outcomes include symptoms, change in disease status, morbid events, functional outcomes, health status measures, quality of life, and treatment-related morbidity. One RCT, the Trial to Assess Chelation Therapy (TACT), reported that chelation therapy reduced cardiovascular events in patients with a previous myocardial infarction and that the benefit was greater in diabetic patients compared with nondiabetic patients. However, this trial had significant limitations, including high dropout rates, and therefore conclusions are not definitive. For other conditions, including, but not limited to, atherosclerosis, autism, Alzheimer's disease, diabetes and arthritis, the available RCTs did not report improvements in health outcomes with chelation therapy and, as evidence, the case series are inadequate to determine efficacy. The evidence is insufficient to determine the effect of the technology on health outcomes.

Practice Guidelines and Position Statements

American College of Physicians et al

In 2012, the American College of Physicians, American College of Cardiology Foundation, American Heart Association, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association and Society of Thoracic Surgeons published a clinical practice guideline on 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 IHD. (Grade: strong recommendation; low-quality evidence)" However, citing the Trial to Assess Chelation Therapy, a 2014 focused update of this guideline included a revised recommendation on chelation therapy, stating that the "usefulness of chelation therapy is uncertain for reducing cardiovascular events in patients with stable IHD." The recommendation was upgraded from class III (no benefit) to class IIb (benefit ≥ risk), and the level of evidence from C (only consensus expert opinion, case studies, or standard of care) to B (data from a single randomized trial or nonrandomized studies).

ACP's 2004 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. (Level of evidence B: Based on evidence from a limited number of randomized trials with small numbers of patients, careful analyses of nonrandomized studies, or observational registries.)"

American College of Cardiology

In 2005, the American College of Cardiology, AHA, and other medical societies stated that chelation "is not indicated for treatment of intermittent claudication and may have harmful adverse effects. (Level of Evidence A: Data derived from multiple randomized clinical trials or meta-analyses.)" In 2013, ACCF and AHA compiled previous ACC/AHA and ACCF/AHA recommendations issued in 2005 and 2011 on the management of peripheral artery disease. The recommendation against chelation therapy remained unchanged.

Canadian Cardiovascular Society
Evidence-based, consensus guidelines from the Canadian Cardiovascular Society in 2014 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.

National Institute for Health and Care Excellence
NICE issued clinical guidance on autism in children and young people in 2013 and autism in adults in 2012. Both documents specifically recommend against the use of chelation therapy for the management of autism.

U.S. Preventive Services Task Force Recommendations
Not applicable

Key Words:
Chelation therapy, toxic metal ions, dimercaprol, edetate calcium disodium, deferoxamine, penicillamine, Succimer, Desferal

Approved by Governing Bodies:
In 1953, calcium-ethylenediaminetetraacetic acid (EDTA; Versenate) was approved by the FDA for lowering blood lead levels among both pediatric and adult patients with lead poisoning. In 1991, Succimer (Chemet) was approved by the FDA for the treatment of lead poisoning in pediatric patients only. FDA approved disodium-EDTA for use in selected patients with hypercalcemia and for use in patients with heart rhythm problems due to intoxication with digitalis. In 2008, FDA withdrew approval of disodium-EDTA due to safety concerns and recommended that other forms of chelation therapy be used.

Several iron chelating agents have received FDA approval.

- Deferoxamine for subcutaneous, intramuscular or intravenous injections was approved for treating acute iron intoxication and chronic iron overload due to transfusion-dependent anemia. Several generic forms of deferoxamine have been approved by the FDA.

- In 2005, deferasirox (Exjade®; Novartis) was approved by FDA and is available as a tablet for oral suspension and is indicated for the treatment of chronic iron overload due to blood transfusions in patients age 2 years and older. Under the accelerated approval program, FDA expanded the indications for deferasirox in 2013 to include treatment of patients age 10 years and older with chronic iron overload due to non-transfusion-dependent thalassemia syndromes and specific liver iron concentration and serum ferritin levels. A generic version of deferasirox tablet for oral suspension has also been approved by FDA. In 2015, an oral tablet formulation for deferasirox (Jadenu™) was approved by FDA. All formulations of deferasirox carry a black box warning because it may cause serious and fatal renal toxicity and failure, hepatic toxicity and failure, and

gastrointestinal hemorrhage. As a result, treatment with deferasirox requires close patient monitoring, including laboratory tests of renal and hepatic function.

- In 2011, the FDA approved the iron chelator deferiprone (Ferriporx®) for the treatment of patients with transfusional overload due to thalassemia syndromes when other chelation therapy is inadequate. Deferiprone is available in tablet and oral solution. Ferriprox® carries a black box warning because it can cause agranulocytosis that can lead to serious infections and death. As a result, absolute neutrophil count should be monitored before and during treatment.

In a June 2014 warning to consumers, FDA advised that FDA-approved chelating agents are available by prescription only. There are no FDA-approved over-the-counter chelation products.

Benefit Application:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.
ITS: Home Policy provisions apply
FEP: Special benefit consideration may apply. Refer to member's benefit plan. FEP does not consider investigational if FDA approved and will be reviewed for medical necessity.

Current Coding:

HCPCS codes:

M0300	IV chelation therapy (chemical endarterectomy)
J0470	Injection, dimercaprol
J0600	Injection, edetate calcium disodium, up to 1,000 mg
J0895	Injection, deferoxamine mesylate, 500 mg
J3520	Edetate disodium (EDTA, Diostate) per 150 mg
S9355	Home infusion therapy, chelation therapy; administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment, per diem.

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Policy History:

Medical Policy Group, December 2002
Medical Policy Administration Committee, January 2003
Available for comment February 6-March 24, 2003
Medical Policy Group, December 2005 **(1)**
Medical Policy Group, January 2006 **(1)**
Medical Policy Administration Committee, February 2006
Available for comment March 1-April 14, 2006
Medical Policy Group, April 2006 **(2)**
Medical Policy Administration Committee, April 2006
Available for comment April 20-June 5, 2006
Medical Policy Group June 2006 **(2)**
Medical Policy Administration Committee, June 2006
Available for comment July 5-August 18, 2006
Medical Policy Group, June 2009 **(1)**
Medical Policy Administration Committee, July 2009
Available for comment July 1-August 14, 2009
Medical Policy Panel, April 2012

Medical Policy Group, April 2012 **(2):** Update Key Points, References, Governing Agencies information
Medical Policy Panel, June 2013
Medical Policy Group, September **(2):** Chronic iron overload due to non-transfusion-dependent thalassemia (NDTD) added to medically necessary statement based on new FDA approval. Secondary prevention in patients with myocardial infarction added to bullet point in investigational statement on atherosclerosis. Key Points and References updated to support policy changes. Old references removed.
Medical Policy Administration Committee, September 2013
Available for comment September 19 through November 2, 2013
Medical Policy Panel, June 2014
Medical Policy Group, June 2014 **(4):** Updated Key Points, Practice and Position Statement and References. No changes to the policy statement at this time.
Medical Policy Panel, June 2015
Medical Policy Group, June 2015 **(4):** Updates to Description, Key Points, Approved Governing Bodies, and References. Reworded Policy statement to clarify Chelation therapy in any form is considered investigational in the inpatient or outpatient setting for any other condition. Also reworded policy statement to clarify treatments associated with non-covered chelation therapy is considered investigational. No change to policy intent.
Medical Policy Panel, February 2016
Medical Policy Group, February 2016 **(4):** Updates to Key Points. Clarified policy statement by adding specific metal toxicities and added commas to separate sickle cell and thalassemia; edited category from therapy to pharmacology.
Medical Policy Panel, February 2017
Medical Policy Group, February 2017 **(4):** Updates to Key Points, Approved by Governing Bodies, and References; From Policy section, removed "Effective for dates of service prior to November 3, 2013" and policy statements pertaining to these dates.
Medical Policy Group, October 2017 **(4):** Added Key Word Desferal. No other changes.
Medical Policy Panel, February 2018
Medical Policy Group, February 2018 **(4):** Updates to Key Points and References. No change to policy statement.
Medical Policy Group, May 2018 **(4):** Added HCPCS code S9355 to Current Coding.
