Medical Policy

BlueCross BlueShield of Kansas
An Independent Licensee of the Blue Cross and Blue Shield Association

Title: Chelation Therapy

Professional
Original Effective Date: October 29, 2009
Revision Date(s): November 19, 2012; March 31, 2014
Current Effective Date: March 31, 2014

Institutional
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DESCRIPTION

Chelation therapy, an established treatment for treating heavy metal toxicities, has been investigated for a variety of other applications including treatment of atherosclerosis, Alzheimer's disease, and autism.

Background

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. For example, desferroxamine is used for patients with iron toxicity, and calcium-ethylenediaminetetraacetic acid (-EDTA) is used for patients with lead poisoning. Note that disodium-EDTA is not recommended for acute lead poisoning due to the increased risk of death from hypocalcemia. (1) 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. Chelation therapy has also been discussed as a treatment for other indications including atherosclerosis, Alzheimer's disease, and autism. For example, EDTA chelation therapy has been proposed in patients with atherosclerosis as a method of decreasing obstruction in the arteries.

Regulatory Status

Calcium-EDTA was approved by the FDA for lowering blood lead levels among patients with lead poisoning. Disodium-EDTA was approved by the FDA for use in selected patients with hypercalcemia and for use in patients with heart rhythm problems due to intoxication with the drug, digitalis. In 2008, the FDA withdrew approval of disodium-EDTA due to safety concerns and recommended that other forms of chelation therapy be used. (2)

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. Deferasirox, approved in 2005, is available as a tablet for oral suspension and is indicated for the treatment of chronic iron overload due to blood transfusions in patients aged 2 years and older. Under the accelerated approval program, the FDA expanded approval of deferasirox in 2013 to include the treatment of patients age 10 and older with chronic iron overload due to nontransfusion-dependent thalassemia (NTDT). In 2011, the FDA approved the iron chelator deferiprone for the treatment of patients with transfusional overload due to thalassemia syndromes when other chelation therapy is inadequate. Deferiprone is available in tablet form for oral use.

POLICY

A. Chelation therapy may be considered **medically necessary** in the treatment of each of the following conditions:
   1. control of ventricular arrhythmias or heart block associated with digitalis toxicity
   2. emergency treatment of hypercalcemia
   3. extreme conditions of metal toxicity
   4. treatment of chronic iron overload due to blood transfusions (transfusional hemosiderosis) and due to nontransfusion-dependent thalassemia (NDTD)
   5. Wilson's disease (hepatolenticular degeneration)
   6. lead poisoning

B. Other applications of chelation therapy are considered **experimental / investigational,** including, but not limited to:
   1. atherosclerosis (i.e., coronary artery disease, secondary prevention in patients with myocardial infarction, or peripheral vascular disease)
   2. multiple sclerosis
   3. arthritis (includes rheumatoid arthritis)
   4. hypoglycemia
   5. autism
   6. Alzheimer's disease
   7. diabetes

RATIONALE

The policy was updated with literature searches using MEDLINE, most recently the literature was searched from the period February 2012 through April 24, 2013.

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

Atherosclerosis

In 2002, a Cochrane review was published evaluating studies on ethylenediaminetetraacetic acid (EDTA) chelation therapy for treating patients with atherosclerotic cardiovascular disease. (3) Five placebo-controlled randomized-controlled trials (RCTs) were identified, none of which reported mortality, non-fatal events, and cerebrovascular vascular events. Four of the 5 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 10 patients, was apparently stopped early due to benefit, but relevant outcome data were not available. The Cochrane reviewers concluded that there was insufficient evidence to draw conclusions of the efficacy of chelation therapy for treating atherosclerosis; additional RCTs that report health outcomes including mortality and cerebrovascular events were needed.

Among the published randomized controlled trials (RCTs), Knudtson and colleagues randomized 84 patients with coronary artery disease and a positive treadmill test to receive EDTA chelation therapy or placebo, 3 hours per treatment twice weekly for 15 weeks, and once per month for an additional 3 months. (4) The main 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, randomized controlled study of EDTA chelation or placebo showed no change in short- or long-term improvement in vasomotor response to EDTA when compared to placebo. (5) Two small randomized trials have also reported no benefit of chelation therapy as a treatment of peripheral arterial disease. (6, 7)

Section summary: Several RCTs have been published on chelation therapy for treating atherosclerosis; these have generally 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.

Autism

Based on similarities between mercury poisoning and autism spectrum disorder symptoms, Bernard and colleagues hypothesized a link between environmental mercury and autism. (8) 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. (9) In 2007, a systematic review by Ng and colleagues concluded that there was no association between mercury poisoning and autism. (10)

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. (11) The author stated the case series suggest that chelation might be a viable form of treatment in some autistic individuals with known elevated heavy metal levels and that this possibility needs to be further investigated in controlled studies.

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

Alzheimer's Disease

A 2008 Cochrane Review evaluated metal protein attenuating compounds (MPAC) for treating Alzheimer's disease (12) The review identified one placebo-controlled RCT. This study, by Richie and colleagues, was published in 2003. Patients were treated with PBT1, an MPAC also known as clioquinol, an anti-fungal medication that crosses the blood-brain barrier. (13) 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.

Further studies of PBT1 have been abandoned in favor of a successor compound, PBT2. Lannfelt and colleagues 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). (14) 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.

Ongoing investigations in chelation therapy for the treatment of Alzheimer's disease and other neurodegenerative diseases include linking a carbohydrate moiety to drug molecules to enhance drug delivery across the blood-brain barrier; this strategy may solve the potential problem of premature and indiscriminate metal binding. In addition, multi-function drugs that not only bind metal but also have significant antioxidant capacity are in development. (15)

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

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. (16) A total of 21/30 (70%) of the participants completed the 12-month follow-up. At 12 months, there was a significantly greater change 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.

Diabetic nephropathy
Chen and colleagues in China investigated the effect of chelation therapy on the progression of diabetic nephropathy in patients with high-normal lead levels. Their 2012 single-blind study included 50 patients with diabetes, high-normal body lead burden (80-6,000 *u*g) and serum creatinine 3.8 mg/dL or lower. (17) At baseline, the mean blood lead level was 6.3 *u*g/dL in the treatment group and 7.1 *u*g/dL in the control group and the mean body lead burden was 151 *u*g for patients in the treatment group and 142 *u*g for patients 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 *u*g/dL. (18) Patients were randomized to 3 months of calcium disodium EDTA or placebo. During the following 24 months, 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 *u*g) 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). The yearly rate of decrease in eGFR was 5.6 mL/min/173 m^2 (standard deviation [SD]: 5.0) in the chelation group and 9.2 mL/min/173 m^2 (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 9 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: 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.

Myocardial infarction (MI)

In 2013, findings of the randomized double-blind multicenter Trial to Assess Chelation Therapy (TACT) study were published. (19) The study included 1,708 individuals, age 50 or older, who had a history of a myocardial infarction at least 6 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). The first 30 infusions were given weekly, and the remaining 10 infusions were given 2 to 8 weeks apart. The primary endpoint was a composite outcome that included death from any cause, reinfarction, stroke, coronary revascularization or hospitalization for angina at 5 years. 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 5-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; the p value was 0.035, which was below the significance threshold required due to multiple (11) interim analyses, 0.036. The most common individual clinical endpoint was coronary revascularization, which occurred in 130 of 839 patients (15%) 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 2 events each in the treatment and control group, including 1 death in each group.

The study is limited by the low follow-up rate, including a greater number of patients who withdrew consent in the placebo group compared to the treatment group. The primary endpoint included components of varying clinical significance, with most of the difference between groups occurring for revascularization events. The primary endpoint barely met the significance threshold and if more patients had been retained in the study and experienced events, results could have differed. Moreover, as noted in an editorial accompanying the 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 clinical care. (20)

Section summary: 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. However, this was not a high-quality trial and therefore the results could have arisen from bias. Further trials that are of high quality are needed to corroborate whether chelation therapy improves outcomes in patients with prior MI.

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.

Summary
Chelation therapy is an established treatment for the medically necessary indications listed in the policy statement, such as treatment of metal toxicity and transfusional hemosiderosis. There is insufficient evidence that chelation therapy improves health outcomes for patients with other conditions including, but not limited to, atherosclerosis, autism, Alzheimer's disease, diabetes and arthritis. Thus, chelation therapy for these other applications is considered investigational.

Practice Guidelines and Position Statements
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). (21) The organizations 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)"

A 2004 clinical practice guideline from the American College of Physicians (22) states 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.)"

In 2005, the American College of Cardiology (23) 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.)"

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT/HCPCS

96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)
96375	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); each additional sequential intravenous push of a new substance/drug (List separately in addition to code for primary procedure)
J0470	Injection, dimercaprol, per 100 mg
J0600	Injection, edetate calcium disodium, up to 1,000 mg

J0895 Injection, deferoxamine mesylate, 500 mg
J3520 Edetate disodium, per 150 mg
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

ICD-9 Diagnoses

275.1 Disorders of copper metabolism
275.42 Hypercalcemia
282.44 Beta thalassemia (thalassemia intermedia)
984.0-984.9 Toxic effect of lead and its compounds (including fumes) (code range)
999.88 Other infusion reaction
999.89 Other transfusion reaction

ICD-10 Diagnoses (Effective October 1, 2014)

E83.01 Wilson's disease
E83.52 Hypercalcemia
T46.0X1A Poisoning by cardiac-stimulant glycosides and drugs of similar action, accidental (unintentional), initial encounter
T46.0X1D Poisoning by cardiac-stimulant glycosides and drugs of similar action, accidental (unintentional), subsequent encounter
T46.0X1S Poisoning by cardiac-stimulant glycosides and drugs of similar action, accidental (unintentional), sequela
T46.0X2A Poisoning by cardiac-stimulant glycosides and drugs of similar action, intentional self-harm, initial encounter
T46.0X2D Poisoning by cardiac-stimulant glycosides and drugs of similar action, intentional self-harm, subsequent encounter
T46.0X2S Poisoning by cardiac-stimulant glycosides and drugs of similar action, intentional self-harm, sequela
T46.0X3A Poisoning by cardiac-stimulant glycosides and drugs of similar action, assault, initial encounter
T46.0X3D Poisoning by cardiac-stimulant glycosides and drugs of similar action, assault, subsequent encounter
T46.0X3S Poisoning by cardiac-stimulant glycosides and drugs of similar action, assault, sequela
T56.0X1A Toxic effect of lead and its compounds, accidental (unintentional), initial encounter
T56.0X1D Toxic effect of lead and its compounds, accidental (unintentional), subsequent encounter
T56.0X1S Toxic effect of lead and its compounds, accidental (unintentional), sequela
T56.0X2A Toxic effect of lead and its compounds, intentional self-harm, initial encounter
T56.0X2D Toxic effect of lead and its compounds, intentional self-harm, subsequent encounter
T56.0X2S Toxic effect of lead and its compounds, intentional self-harm, sequela
T56.0X3A Toxic effect of lead and its compounds, assault, initial encounter
T56.0X3D Toxic effect of lead and its compounds, assault, subsequent encounter
T56.0X3S Toxic effect of lead and its compounds, assault, sequela

T56.1X1A	Toxic effect of mercury and its compounds, accidental (unintentional), initial encounter
T56.1X1D	Toxic effect of mercury and its compounds, accidental (unintentional), subsequent encounter
T56.1X1S	Toxic effect of mercury and its compounds, accidental (unintentional), sequela
T56.1X2A	Toxic effect of mercury and its compounds, intentional self-harm, initial encounter
T56.1X2D	Toxic effect of mercury and its compounds, intentional self-harm, subsequent encounter
T56.1X2S	Toxic effect of mercury and its compounds, intentional self-harm, sequela
T56.1X3A	Toxic effect of mercury and its compounds, assault, initial encounter
T56.1X3D	Toxic effect of mercury and its compounds, assault, subsequent encounter
T56.1X3S	Toxic effect of mercury and its compounds, assault, sequela
T56.2X1A	Toxic effect of chromium and its compounds, accidental (unintentional), initial encounter
T56.2X1D	Toxic effect of chromium and its compounds, accidental (unintentional), subsequent encounter
T56.2X1S	Toxic effect of chromium and its compounds, accidental (unintentional), sequela
T56.2X2A	Toxic effect of chromium and its compounds, intentional self-harm, initial encounter
T56.2X2D	Toxic effect of chromium and its compounds, intentional self-harm, subsequent encounter
T56.2X2S	Toxic effect of chromium and its compounds, intentional self-harm, sequela
T56.2X3A	Toxic effect of chromium and its compounds, assault, initial encounter
T56.2X3D	Toxic effect of chromium and its compounds, assault, subsequent encounter
T56.2X3S	Toxic effect of chromium and its compounds, assault, sequela
T56.3X1A	Toxic effect of cadmium and its compounds, accidental (unintentional), initial encounter
T56.3X1D	Toxic effect of cadmium and its compounds, accidental (unintentional), subsequent encounter
T56.3X1S	Toxic effect of cadmium and its compounds, accidental (unintentional), sequela
T56.3X2A	Toxic effect of cadmium and its compounds, intentional self-harm, initial encounter
T56.3X2D	Toxic effect of cadmium and its compounds, intentional self-harm, subsequent encounter
T56.3X2S	Toxic effect of cadmium and its compounds, intentional self-harm, sequela
T56.3X3A	Toxic effect of cadmium and its compounds, assault, initial encounter
T56.3X3D	Toxic effect of cadmium and its compounds, assault, subsequent encounter
T56.3X3S	Toxic effect of cadmium and its compounds, assault, sequela
T56.4X1A	Toxic effect of copper and its compounds, accidental (unintentional), initial encounter
T56.4X1D	Toxic effect of copper and its compounds, accidental (unintentional), subsequent encounter
T56.4X1S	Toxic effect of copper and its compounds, accidental (unintentional), sequela
T56.4X2A	Toxic effect of copper and its compounds, intentional self-harm, initial encounter
T56.4X2D	Toxic effect of copper and its compounds, intentional self-harm, subsequent encounter
T56.4X2S	Toxic effect of copper and its compounds, intentional self-harm, sequela
T56.4X3A	Toxic effect of copper and its compounds, assault, initial encounter
T56.4X3D	Toxic effect of copper and its compounds, assault, subsequent encounter
T56.4X3S	Toxic effect of copper and its compounds, assault, sequela

T56.5X1A	Toxic effect of zinc and its compounds, accidental (unintentional), initial encounter
T56.5X1D	Toxic effect of zinc and its compounds, accidental (unintentional), subsequent encounter
T56.5X1S	Toxic effect of zinc and its compounds, accidental (unintentional), sequela
T56.5X2A	Toxic effect of zinc and its compounds, intentional self-harm, initial encounter
T56.5X2D	Toxic effect of zinc and its compounds, intentional self-harm, subsequent encounter
T56.5X2S	Toxic effect of zinc and its compounds, intentional self-harm, sequela
T56.5X3A	Toxic effect of zinc and its compounds, assault, initial encounter
T56.5X3D	Toxic effect of zinc and its compounds, assault, subsequent encounter
T56.5X3S	Toxic effect of zinc and its compounds, assault, sequela
T56.6X1A	Toxic effect of tin and its compounds, accidental (unintentional), initial encounter
T56.6X1D	Toxic effect of tin and its compounds, accidental (unintentional), subsequent encounter
T56.6X1S	Toxic effect of tin and its compounds, accidental (unintentional), sequela
T56.6X2A	Toxic effect of tin and its compounds, intentional self-harm, initial encounter
T56.6X2D	Toxic effect of tin and its compounds, intentional self-harm, subsequent encounter
T56.6X2S	Toxic effect of tin and its compounds, intentional self-harm, sequela
T56.6X3A	Toxic effect of tin and its compounds, assault, initial encounter
T56.6X3D	Toxic effect of tin and its compounds, assault, subsequent encounter
T56.6X3S	Toxic effect of tin and its compounds, assault, sequela
T56.7X1A	Toxic effect of beryllium and its compounds, accidental (unintentional), initial encounter
T56.7X1D	Toxic effect of beryllium and its compounds, accidental (unintentional), subsequent encounter
T56.7X1S	Toxic effect of beryllium and its compounds, accidental (unintentional), sequela
T56.7X2A	Toxic effect of beryllium and its compounds, intentional self-harm, initial encounter
T56.7X2D	Toxic effect of beryllium and its compounds, intentional self-harm, subsequent encounter
T56.7X2S	Toxic effect of beryllium and its compounds, intentional self-harm, sequela
T56.7X3A	Toxic effect of beryllium and its compounds, assault, initial encounter
T56.7X3D	Toxic effect of beryllium and its compounds, assault, subsequent encounter
T56.7X3S	Toxic effect of beryllium and its compounds, assault, sequela
T56.811A	Toxic effect of thallium, accidental (unintentional), initial encounter
T56.811D	Toxic effect of thallium, accidental (unintentional), subsequent encounter
T56.811S	Toxic effect of thallium, accidental (unintentional), sequela
T56.812A	Toxic effect of thallium, intentional self-harm, initial encounter
T56.812D	Toxic effect of thallium, intentional self-harm, subsequent encounter
T56.812S	Toxic effect of thallium, intentional self-harm, sequela
T56.813A	Toxic effect of thallium, assault, initial encounter
T56.813D	Toxic effect of thallium, assault, subsequent encounter
T56.813S	Toxic effect of thallium, assault, sequela
T56.891A	Toxic effect of other metals, accidental (unintentional), initial encounter
T56.891D	Toxic effect of other metals, accidental (unintentional), subsequent encounter
T56.891S	Toxic effect of other metals, accidental (unintentional), sequela
T56.892A	Toxic effect of other metals, intentional self-harm, initial encounter
T56.892D	Toxic effect of other metals, intentional self-harm, subsequent encounter
T56.892S	Toxic effect of other metals, intentional self-harm, sequela
T56.893A	Toxic effect of other metals, assault, initial encounter

T56.893D	Toxic effect of other metals, assault, subsequent encounter
T56.893S	Toxic effect of other metals, assault, sequela
T56.91XA	Toxic effect of unspecified metal, accidental (unintentional), initial encounter
T56.91XD	Toxic effect of unspecified metal, accidental (unintentional), subsequent encounter
T56.91XS	Toxic effect of unspecified metal, accidental (unintentional), sequela
T56.92XA	Toxic effect of unspecified metal, intentional self-harm, initial encounter
T56.92XD	Toxic effect of unspecified metal, intentional self-harm, subsequent encounter
T56.92XS	Toxic effect of unspecified metal, intentional self-harm, sequela
T56.93XA	Toxic effect of unspecified metal, assault, initial encounter
T56.93XD	Toxic effect of unspecified metal, assault, subsequent encounter
T56.93XS	Toxic effect of unspecified metal, assault, sequela
T80.89XA	Other complications following infusion, transfusion and therapeutic injection, initial encounter
T80.89XD	Other complications following infusion, transfusion and therapeutic injection, subsequent encounter
T80.89XS	Other complications following infusion, transfusion and therapeutic injection, sequela
T80.90XA	Unspecified complication following infusion and therapeutic injection, initial encounter
T80.90XD	Unspecified complication following infusion and therapeutic injection, subsequent encounter
T80.90XS	Unspecified complication following infusion and therapeutic injection, sequela

REVISIONS

11-19-2012	Policy added to the bcbsks.com web site.
	Effective for Institutional providers 12-19-2012.
03-31-2014	Description section updated
	In Policy section: ▪ Added to A 4 "and due to nontransfusion-dependent thalassemia (NDTD)" to read, "4. treatment of chronic iron overload due to blood transfusions (transfusional hemosiderosis) and due to nontransfusion-dependent thalassemia (NDTD)" ▪ Added to B 1 "secondary prevention in patients with myocardial infarction" to read, "1. atherosclerosis (i.e., coronary artery disease, secondary prevention in patients with myocardial infarction, or peripheral vascular disease)"
	Rationale section updated
	In Coding section: ▪ Removed ICD-9 Diagnoses Codes: 427.9, 440.0-440.9 ▪ Added ICD-10 Diagnoses Codes
	References updated

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