MEDICAL POLICY

POLICY TITLE	INTRAVENOUS CHELATION THERAPY
POLICY NUMBER	MP 4.005

CLINICAL BENEFIT	☐ MINIMIZE SAFETY RISK OR CONCERN. ☐ MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. ☐ ASSURE APPROPRIATE LEVEL OF CARE. ☐ ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. ☒ ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. ☐ ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
Effective Date:	**4/1/2026**

POLICY

Dimercaprol (BAL in Oil) may be considered **medically necessary** for one of the following indications:

- Treatment of arsenic, gold, or mercury toxicity
- Acute lead poisoning when used on concomitantly with Edetate Calcium Disodium injection
- Acute poisoning by mercury salts if therapy begins within one- or two-hours following ingestion

All other indications are considered **investigational.** There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure for these indications.

Edetate Calcium Disodium (Calcium EDTA) may be considered **medically necessary** for the following:

- Reduction of blood levels and depot stores of lead in lead poisoning (acute and chronic) and lead encephalopathy

All other indications are considered **investigational.** There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure for these indications.

Deferoxamine mesylate (Desferal®) may be considered **medically necessary** for one of the following indications:

- Acute iron toxicity
- Chronic iron toxicity due to transfusion-dependent anemias

All other indications are considered **investigational.** There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure for these indications.

FDA removed the approval for NaEDTA as chelation therapy due to safety concerns. Its use is considered **investigational.**

Off-label applications of chelation therapy are considered **investigational**, including, but not limited to:

- Atherosclerosis/arteriosclerosis (e.g., coronary artery disease, secondary prevention in patients with myocardial infarction, or peripheral vascular disease);
- Multiple sclerosis;
- Arthritis (including rheumatoid arthritis);
- Autism Spectrum Disorders;
- Alzheimer's disease;
- Diabetes.

There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure for these indications.

POLICY GUIDELINES

Due to pharmacological property differences and mechanisms of action, each chelation agent only be used as indicated in accordance with the FDA label.

For the below 2 bullet points, most patients should be treated with other modalities. Digitalis toxicity is currently treated in most patients with Fab monoclonal antibodies. The FDA removed the approval for NaEDTA as chelation therapy due to safety concerns and recommended that other chelators be used.

- control of ventricular arrhythmias or heart block associated with digitalis toxicity
- emergency treatment of hypercalcemia.

Suggested toxic or normal levels of select heavy metals are listed in Table 1.

Suggested Toxic or Normal Concentrations of Heavy Metals Table 1

Metal	Toxic Levels (Normal Levels Where Indicated)
Arsenic	24-h urine: greater than or equal to 50 µg/L urine or 100 µg/g creatinine
Bismuth	No clear reference standard
Cadmium	Proteinuria and/or greater than or equal to 15 µg/g creatinine
Chromium	No clear reference standard
Cobalt	Normative excretion: 0.1-1.2 µg/L (serum), 0.1-2.2 µg/L (urine)
Copper	Normative excretion: 25 µg/24 h (urine)
Iron	• Nontoxic: less than 300 µg/dL • Severe: greater than 500 µg/dL
Lead	Pediatric • Symptoms or blood lead level greater than or equal to 45 µg/dL (blood) • CDC level of concern: 5 µg/dL

Metal	Toxic Levels (Normal Levels Where Indicated)
	Adult • Symptoms or blood lead level greater than or equal to 70 µg/dL CDC level of concern: 10 µg/dL
Manganese	No clear reference standard
Mercury	Background exposure normative limits: 1-8 µg/L (whole blood); 4-5 µg/L (urine)
Nickel	• Excessive exposure: greater than or equal to 8 µg/L (blood) • Severe poisoning: greater than or equal to 500 µg/L (8-h urine)
Selenium	• Mild toxicity: greater than 1 µg/L (serum); • Serious toxicity: greater than 2 µg/L
Silver	Asymptomatic workers have mean levels of 11 µg/L (serum) and 2.6 µg/L (spot urine)
Thallium	24-hour urine thallium greater than 5 µg/L
Zinc	Normative range: 0.6-1.1 mg/L (plasma), 10-14 µg/L (red cells)

Adapted from Adal (2018) CDC: Centers for Disease Control and Prevention

A hair analysis is useful to assess mercury exposure in epidemiologic studies. However, hair analysis in individual patients must be interpreted with consideration of the patient's history, signs, and symptoms, and possible alternative explanations. Measurement of blood and urine mercury levels can exclude exogenous contamination; therefore, blood or urine mercury levels may be more robust measures of exposure in individual patients.

Cross-reference:

MP 2.304 Autism Spectrum Disorders
MP 2.312 Genetic Testing for Hereditary Hemochromatosis

PRODUCT VARIATIONS

TOP

This policy is only applicable to certain programs and products administered by Capital Blue Cross and subject to benefit variations. Please see additional information below.

FEP PPO- Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at:

https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies .

DESCRIPTION/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 comprises 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, desferrioxamine (not FDA-approved) is used for patients with iron toxicity, and calcium-ethylenediaminetetraacetic acid (EDTA) is used for patients with lead poisoning. (Disodium-EDTA is not recommended for acute lead poisoning due to the increased risk of death from hypocalcemia.)

Another class of chelating agents, called metal protein attenuating compounds (MPACs), is under investigation for the treatment of Alzheimer 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 disease, they promote the solubilization and clearance of beta amyloid by binding its metal-ion complex and also inhibit redox reactions that generate neurotoxic free radicals. MPACs therefore interrupt 2 putative pathogenic processes of Alzheimer disease. However, no MPACs have received FDA approval for the treatment of Alzheimer disease.

Chelation therapy also has been discussed as a treatment for other indications including atherosclerosis 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

In 1953, EDTA (Versenate) was approved by the U.S. Food and Drug Administration (FDA) for lowering blood lead levels among both pediatric and adult patients with lead poisoning. In 1991, succimer (Chemet) was approved by FDA for the treatment of lead poisoning in pediatric patients only. The 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 are FDA-approved:

- In 1968, deferoxamine (Desferal®; Novartis) was approved by FDA for subcutaneous, intramuscular, or intravenous injections to treat acute iron intoxication and chronic iron overload due to transfusion-dependent anemia. Several generic forms of deferoxamine have been approved by FDA.
- In 2005, deferasirox (Exjade®; Novartis) was approved by FDA, is available as a tablet for oral suspension, and is indicated for the treatment of chronic iron overload due to blood transfusions in patients ages 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 iron chelator deferiprone (Ferriprox®) was approved by FDA for treatment of patients with transfusional overload due to thalassemia syndromes when another 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 would be available by prescription only. There are no FDA-approved over-the-counter chelation products.

RATIONALE

SUMMARY OF EVIDENCE

For individuals who have Alzheimer disease, or cardiovascular disease, or autism spectrum disorder, or diabetes, or multiple sclerosis, or arthritis who receive chelation therapy, the evidence includes a small number of RCTs and case series. Relevant outcomes are 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) reported that chelation therapy reduced cardiovascular events in patients with previous myocardial infarction and that the benefit was greater in diabetic patients compared with nondiabetic patients. However, this trial had significant limitations (e.g., high dropout rates) and, therefore, conclusions are not definitive. For other conditions, 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.

DEFINITIONS

HEAVY METALS refer to metals such as mercury, lead, chromium, arsenic, and cadmium, which have known toxic effects on internal organs (i.e. kidneys, brain, bone, retina).

HEMOCHROMATOSIS is a genetic disease marked by excessive absorption and accumulation of iron into the body.

THALASSEMIA refers to a group of hereditary anemias occurring in populations bordering the Mediterranean and in Southeast Asia.

MEDICAL POLICY

POLICY TITLE	INTRAVENOUS CHELATION THERAPY
POLICY NUMBER	MP 4.005

DISCLAIMER

Capital Blue Cross' medical policies are used to determine coverage for specific medical technologies, procedures, equipment, and services. These medical policies do not constitute medical advice and are subject to change as permitted by law or applicable clinical evidence from independent treatment guidelines. Treating providers are solely responsible for medical advice and treatment of members. These polices are not a guarantee of coverage or payment. Payment of claims is subject to a determination regarding the member's benefit program and eligibility on the date of service, and a determination that the services are medically necessary and appropriate. Final processing of a claim is based upon the terms of contract that applies to the members' benefit program, including benefit limitations and exclusions. If a provider or a member has a question concerning this medical policy, please contact Capital Blue Cross' Provider Services or Member Services.

CODING INFORMATION

Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Investigational for all indications:

Procedure Codes	Description
M0300	IV chelation therapy (chemical endarterectomy)

NaEDTA is considered investigational as FDA has removed approval for its use with chelation therapy; therefore, not covered:

Procedure Codes	Description
J3520	Edetate disodium, per 150 mg

Covered when medically necessary:

Procedure codes						
J0470	S9355					

ICD-10 CM Diagnosis Code	Description
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
T56.0X2A	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
T56.0X3A	Toxic effect of lead and its compounds, assault, initial encounter
T56.0X3D	Toxic effect of lead and its compounds, assault, subsequent encounter
T56.0X4A	Toxic effect of lead and its compounds, undetermined, initial encounter
T56.0X4D	Toxic effect of lead and its compounds, undetermined, subsequent encounter
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
T56.1X2A	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
T56.1X3A	Toxic effect of mercury and its compounds, assault, initial encounter
T56.1X3D	Toxic effect of mercury and its compounds, assault, subsequent encounter
T56.1X4A	Toxic effect of mercury and its compounds, undetermined, initial encounter
T56.1X4D	Toxic effect of mercury and its compounds, undetermined, subsequent encounter
T56.891A	Toxic effect of other metals, accidental (unintentional), initial encounter
T56.891D	Toxic effect of other metals, accidental (unintentional), subsequent encounter
T56.892A	Toxic effect of other metals, intentional self-harm, initial encounter
T56.892D	Toxic effect of other metals, intentional self-harm, subsequent encounter
T56.893A	Toxic effect of other metals, assault, initial encounter
T56.893D	Toxic effect of other metals, assault, subsequent encounter
T56.894A	Toxic effect of other metals, undetermined, initial encounter
T56.894D	Toxic effect of other metals, undetermined, subsequent encounter
T56.94XA	Toxic effect of unspecified metal, undetermined, initial encounter
T56.94XD	Toxic effect of unspecified metal, undetermined, subsequent encounter

ICD-10 CM Diagnosis Code	Description
T57.0X1A	Toxic effect of arsenic and its compounds, accidental (unintentional), initial encounter
T57.0X1D	Toxic effect of arsenic and its compounds, accidental (unintentional), subsequent encounter
T57.0X2A	Toxic effect of arsenic and its compounds, intentional self-harm, initial encounter
T57.0X2D	Toxic effect of arsenic and its compounds, intentional self-harm, subsequent encounter
T57.0X3A	Toxic effect of arsenic and its compounds, assault, initial encounter
T57.0X3D	Toxic effect of arsenic and its compounds, assault, subsequent encounter
T57.0X4A	Toxic effect of arsenic and its compounds, undetermined, initial encounter
T57.0X4D	Toxic effect of arsenic and its compounds, undetermined, subsequent encounter
R78.79	Finding of abnormal level of heavy metals in blood

Procedure codes						
J0600	S9355					

ICD-10 CM Diagnosis Codes	Description
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
T56.0X2A	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
T56.0X3A	Toxic effect of lead and its compounds, assault, initial encounter
T56.0X3D	Toxic effect of lead and its compounds, assault, subsequent encounter
T56.0X4A	Toxic effect of lead and its compounds, undetermined, initial encounter
T56.0X4D	Toxic effect of lead and its compounds, undetermined, subsequent encounter
T56.891A	Toxic effect of other metals, accidental (unintentional), initial encounter
T56.891D	Toxic effect of other metals, accidental (unintentional), subsequent encounter
T56.892A	Toxic effect of other metals, intentional self-harm, initial encounter
T56.892D	Toxic effect of other metals, intentional self-harm, subsequent encounter
T56.893A	Toxic effect of other metals, assault, initial encounter
T56.893D	Toxic effect of other metals, assault, subsequent encounter

POLICY TITLE	INTRAVENOUS CHELATION THERAPY
POLICY NUMBER	MP 4.005

ICD-10 CM Diagnosis Codes	Description
T56.894A	Toxic effect of other metals, undetermined, initial encounter
T56.894D	Toxic effect of other metals, undetermined, subsequent encounter
T56.94XA	Toxic effect of unspecified metal, undetermined, initial encounter
T56.94XD	Toxic effect of unspecified metal, undetermined, subsequent encounter
R78.71	Abnormal lead level in blood
R78.79	Finding of abnormal level of heavy metals in blood

Procedure codes						
J0895	S9355					

ICD-10 CM Diagnosis Codes	Description
T45.4X1A	Poisoning by iron and its compounds, accidental (unintentional), initial encounter
T45.4X1D	Poisoning by iron and its compounds, accidental (unintentional), subsequent encounter
T45.4X2A	Poisoning by iron and its compounds, intentional self-harm, initial encounter
T45.4X2D	Poisoning by iron and its compounds, intentional self-harm, subsequent encounter
T45.4X3A	Poisoning by iron and its compounds, assault, initial encounter
T45.4X3D	Poisoning by iron and its compounds, assault, subsequent encounter
T45.4X4A	Poisoning by iron and its compounds, undetermined, initial encounter
T45.4X4D	Poisoning by iron and its compounds, undetermined, subsequent encounter
T56.891A	Toxic effect of other metals, accidental (unintentional), initial encounter
T56.891D	Toxic effect of other metals, accidental (unintentional), subsequent encounter
T56.892A	Toxic effect of other metals, intentional self-harm, initial encounter
T56.892D	Toxic effect of other metals, intentional self-harm, subsequent encounter
T56.893A	Toxic effect of other metals, assault, initial encounter
T56.893D	Toxic effect of other metals, assault, subsequent encounter
T56.894A	Toxic effect of other metals, undetermined, initial encounter
T56.894D	Toxic effect of other metals, undetermined, subsequent encounter
T56.94XA	Toxic effect of unspecified metal, undetermined, initial encounter
T56.94XD	Toxic effect of unspecified metal, undetermined, subsequent encounter
D56.0	Alpha thalassemia
D56.1	Beta thalassemia
D56.2	Delta-beta thalassemia

POLICY TITLE	INTRAVENOUS CHELATION THERAPY
POLICY NUMBER	MP 4.005

ICD-10 CM Diagnosis Codes	Description
D56.3	Thalassemia minor
D56.5	Hemoglobin E-beta thalassemia
D56.8	Other thalassemias
D56.9	Thalassemia, unspecified
E83.111	Hemochromatosis due to repeated red blood cell transfusions

REFERENCES

1. *Centers for Disease Control and Prevention (CDC). Deaths associated with hypocalcemia from chelation therapy--Texas, Pennsylvania, and Oregon, 2003-2005. MMWR Morb Mortal Wkly Rep. Mar 03, 2006; 55(8): 204-7. PMID 16511441*
2. *Food and Drug Administration. Hospira, Inc., et al.; Withdrawal of Approval of One New Drug Application and Two Abbreviated New Drug Application. Federal Register. 2008;73(113):33440-33441.*
3. *Sampson E, Jenagaratnam L, McShane R. Metal protein attenuating compounds for the treatment of Alzheimer's disease. Cochrane Database Syst Rev. Jan 23, 2008; (1): CD005380. PMID 18254079*
4. *Ritchie CW, Bush AI, Mackinnon A, et al. Metal-protein attenuation with iodochlorhydroxyquin (clioquinol) targeting Abeta amyloid deposition and toxicity in Alzheimer disease: a pilot phase 2 clinical trial. Arch Neurol. Dec 2003; 60(12): 1685-91. PMID 14676042*
5. *Sampson EL, Jenagaratnam L, McShane R. Metal protein attenuating compounds for the treatment of Alzheimer's dementia. Cochrane Database Syst Rev. May 16, 2012; (5): CD005380. PMID 22592705*
6. *Lannfelt L, Blennow K, Zetterberg H, et al. Safety, efficacy, and biomarker findings of PBT2 in targeting Abeta as a modifying therapy for Alzheimer's disease: a phase IIa, double-blind, randomised, placebo-controlled trial. Lancet Neurol. Sep 2008; 7(9): 779-86. PMID 18672400*
7. *Villarruz-Sulit MV, Forster R, Dans AL, et al. Chelation therapy for atherosclerotic cardiovascular disease. Cochrane Database Syst Rev. May 05, 2020; 5: CD002785. PMID 32367513*
8. *Lamas GA, Goertz C, Boineau R, et al. Effect of disodium EDTA chelation regimen on cardiovascular events in patients with previous myocardial infarction: the TACT randomized trial. JAMA. Mar 27, 2013; 309(12): 1241-50. PMID 23532240*
9. *Mark DB, Anstrom KJ, Clapp-Channing NE, et al. Quality-of-life outcomes with a disodium EDTA chelation regimen for coronary disease: results from the trial to assess chelation therapy randomized trial. Circ Cardiovasc Qual Outcomes. Jul 2014; 7(4): 508-16. PMID 24987051*
10. *Lamas GA, Boineau R, Goertz C, et al. EDTA chelation therapy alone and in combination with oral high-dose multivitamins and minerals for coronary disease: The*

factorial group results of the Trial to Assess Chelation Therapy. Am Heart J. Jul 2014; 168(1): 37-44.e5. PMID 24952858

11. *Lewis EF, Ujueta F, Lamas GA, et al. Differential Outcomes with Edetate Disodium-Based Treatment Among Stable Post Anterior vs. Non-Anterior Myocardial Infarction Patients. Cardiovasc Revasc Med. Nov 2020; 21(11): 1389-1395. PMID 32303436*
12. *Nissen SE. Concerns about reliability in the Trial to Assess Chelation Therapy (TACT). JAMA. Mar 27, 2013; 309(12): 1293-4. PMID 23532246*
13. *Maron DJ, Hlatky MA. Trial to Assess Chelation Therapy (TACT) and equipoise: When evidence conflicts with beliefs. Am Heart J. Jul 2014; 168(1): 4-5. PMID 24952853*
14. *Bernard S, Enayati A, Redwood L, et al. Autism: a novel form of mercury poisoning. Med Hypotheses. Apr 2001; 56(4): 462-71. PMID 11339848*
15. *Nelson KB, Bauman ML. Thimerosal and autism?. Pediatrics. Mar 2003; 111(3): 674-9. PMID 12612255*
16. *Ng DK, Chan CH, Soo MT, et al. Low-level chronic mercury exposure in children and adolescents: meta-analysis. Pediatr Int. Feb 2007; 49(1): 80-7. PMID 17250511*
17. *Rossignol DA. Novel and emerging treatments for autism spectrum disorders: a systematic review. Ann Clin Psychiatry. Oct-Dec 2009; 21(4): 213-36. PMID 19917212*
18. *Cooper GJ, Young AA, Gamble GD, et al. A copper (II)-selective chelator ameliorates left-ventricular hypertrophy in type 2 diabetic patients: a randomised placebo-controlled study. Diabetologia. Apr 2009; 52(4): 715-22. PMID 19172243*
19. *Escolar E, Lamas GA, Mark DB, et al. The effect of an EDTA-based chelation regimen on patients with diabetes mellitus and prior myocardial infarction in the Trial to Assess Chelation Therapy (TACT). Circ Cardiovasc Qual Outcomes. Jan 2014; 7(1): 15-24. PMID 24254885*
20. *Ujueta F, Arenas IA, Escolar E, et al. The effect of EDTA-based chelation on patients with diabetes and peripheral artery disease in the Trial to Assess Chelation Therapy (TACT). J Diabetes Complications. Jul 2019; 33(7): 490-494. PMID 31101487*
21. *Escolar E, Ujueta F, Kim H, et al. Possible differential benefits of edetate disodium in post-myocardial infarction patients with diabetes treated with different hypoglycemic strategies in the Trial to Assess Chelation Therapy (TACT). J Diabetes Complications. Aug 2020; 34(8): 107616. PMID 32446881*
22. *Chen KH, Lin JL, Lin-Tan DT, et al. Effect of chelation therapy on progressive diabetic nephropathy in patients with type 2 diabetes and high-normal body lead burdens. Am J Kidney Dis. Oct 2012; 60(4): 530-8. PMID 22721929*
23. *U.S. Department of Labor, Occupational Health and Safety Administration. Safety and Health Regulations for Construction: Substance Data Sheet for Occupational Exposure to Lead. 1993.*
24. *Weinreb O, Mandel S, Youdim MBH, et al. Targeting dysregulation of brain iron homeostasis in Parkinson's disease by iron chelators. Free Radic Biol Med. Sep 2013; 62: 52-64. PMID 23376471*
25. *Grolez G, Moreau C, Sablonniere B, et al. Ceruloplasmin activity and iron chelation treatment of patients with Parkinson's disease. BMC Neurol. May 06, 2015; 15: 74. PMID 25943368*

26. *van Eijk LT, Heemskerk S, van der Pluijm RW, et al. The effect of iron loading and iron chelation on the innate immune response and subclinical organ injury during human endotoxemia: a randomized trial. Haematologica. Mar 2014; 99(3): 579-87. PMID 24241495*
27. *Gerhard-Herman MD, Gornik HL, Barrett C, et al. 2016 AHA/ACC Guideline on the Management of Patients with Lower Extremity Peripheral Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. Mar 21, 2017; 135(12): e726-e779. PMID 27840333*
28. *Fihn SD, Blankenship JC, Alexander KP, et al. 2014 ACC/AHA/AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol. Nov 04, 2014; 64(18): 1929-49. PMID 25077860*
29. *Qaseem A, Fihn SD, Dallas P, et al. Management of stable ischemic heart disease: summary of a clinical practice guideline from the American College of Physicians/American College of Cardiology Foundation/American Heart Association/American Association for Thoracic Surgery/Preventive Cardiovascular Nurses Association/Society of Thoracic Surgeons. Ann Intern Med. Nov 20, 2012; 157(10): 735-43. PMID 23165665*
30. *Hyman SL, Levy SE, Myers SM, et al. Identification, Evaluation, and Management of Children with Autism Spectrum Disorder. Pediatrics. Jan 2020; 145(1). PMID 31843864*
31. *Centers for Medicare & Medicaid Services (CMS). National Coverage Determination (NCD) for CHELATION THERAPY for Treatment of Atherosclerosis (20.21). n.d.;*
32. *Centers for Medicare & Medicaid Services (CMS). National Coverage Determination (NCD) for Ethylenediamine- Tetra-Acetic (EDTA) CHELATION THERAPY for Treatment of Atherosclerosis (20.22).*
33. *Centers for Disease Control and Prevention (CDC). What Do Parents Need to Know to Protect Their Children? 2017, May 17.*
34. *Centers for Disease Control and Prevention (CDC). Very high blood lead levels among adults - United States, 2002-2011. MMWR Morb Mortal Wkly Rep. Nov 29, 2013; 62(47): 967-71. PMID 24280917*
35. *Centers for Disease Control and Prevention, Childhood Lead Poisoning Prevention; Recommended Actions Based on Blood Lead Level. April 17, 2024.*
36. *Agency for Toxic Substances and Disease Registry. Toxicological profile for mercury. 1999 March.*
37. *Centers for Disease Control and Prevention (CDC). Emergency preparedness and response. Case definition: thallium. 2015 November 18.*
38. *Adal A. Medscape. Heavy metal toxicity. 2018; http://emedicine.medscape.com/article/814960-overview.*
39. *Kempson IM, Lombi E. Hair analysis as a biomonitor for toxicology, disease and health status. Chem Soc Rev. Jul 2011; 40(7): 3915-40. PMID 21468435*

40. Ravalli F, Vela Parada X, Ujueta F, et al. Chelation Therapy in Patients with Cardiovascular Disease: A Systematic Review. J Am Heart Assoc. Mar 15, 2022; 11(6): e024648. PMID 35229619
41. Devos D, Labreuche J, Rascol O, et al. Trial of Deferiprone in Parkinson's Disease. N Engl J Med. Dec 01, 2022; 387(22): 2045-2055. PMID 36449420.
42. Vichinsky EP, Iron Chelators: Choice of agent, dosing, and adverse effects. In UpToDate Online Journal. [serial online]. Waltham, MA: UpToDate. Updated Sep 24, 2024, 2022.Literature review through Sep 2024.
43. Goldman RH, HU H. Lead exposure, toxicity, and poisoning in adults. In UpToDate Online Journal. [serial online]. Waltham, MA: UpToDate. Updated Jan 12 2023,. Literature review current through Sep 2024.
44. Bruzzese A, Martino EA, Mendicino F et al. Iron chelation therapy. European Journal of Haematology. 2023 May: 110(5):490-497.
45. Food and Drug Administration. Desferal® deferoxamine mesylate for injection USP. Package Insert.
46. Food and Drug Administration. Calcium Disodium Versenate (edetate calcium disodium injection, USP) Package Insert.
47. Food and Drug Administration. BAL in Oil Ampules DIMERCAPROL INJECTION, USP Package Insert.
48. Levine, M, O'Connor, A: Digitalis (cardiac glycoside) poisoning. In UpToDate Online Journal [serial online]. Waltham, MA. UpToDate; Updated June 2024.

POLICY HISTORY

MP 4.005	**08/12/2020 Consensus Review**. No change to policy statements. References updated; Heavy Metal Label Table revised. Coding reviewed dx codes I49.8 and I49.9 added, T56.1XC1S and T56.6X1S removed.
	07/29/2021 Consensus Review. No change to policy statement. References reviewed and updated.
	07/28/2022 Administrative Update. Deleted code I47.2. Effective 10/01/2022
	12/09/2022 Minor Review. Revised the MN criteria to be specific to each chelation therapy. Updated coding to match. References updated.
	08/22/2023 Consensus Review. No change to policy statement. References reviewed and updated. No change to coding.
	10/09/2024 Consensus Review. No change to policy statement. References reviewed and updated. No coding changes.
	08/27/2025 Consensus Review. No change to policy statement.
	02/20/2026 Administrative Update. Updated language to investigational from not medically necessary for coding tables.

POLICY TITLE	INTRAVENOUS CHELATION THERAPY
POLICY NUMBER	MP 4.005

Company® and Keystone Health Plan® Central. Independent licensees of the Blue Cross BlueShield Association. Communications issued by Capital Blue Cross in its capacity as administrator of programs and provider relations for all companies.