



## Clinical Policy: Chelation Therapy

Reference Number: HNCA.CP.MP. 418

Effective Date: 04/08

Last Review Date: 10/19

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### Description

Chelation therapy involves the use of chemical compounds injected into the blood stream, muscle or taken orally to bind undesirable ionic material (eg., heavy metals such as iron, copper, lead and aluminum) that are present in toxic concentrations, so they can be excreted from the body. Examples include

### Policy/Criteria

- I. It is the policy of Health Net of California that chelation therapy may be medically necessary for the following indications:
  - A. For treatment of chronic iron overload in patients with transfusion-dependent anemias (e.g., thalassemias, sickle cell anemia, Cooley's anemia, myelodysplastic syndrome) or secondary hemochromatosis; or
  - B. For treatment of heavy metal overload or toxicity (e.g., lead, arsenic, mercury, iron, copper, or gold) confirmed by appropriate laboratory results (e.g., blood, plasma, and/or urine) and clinical findings consistent with metal toxicity; or
  - C. For treatment of copper overload/toxicity secondary to diseases such as Wilson's disease; or
  - D. For aluminum overload in persons with end-stage renal failure secondary to hemodialysis; or
  - E. For emergency treatment of hypercalcemia; or
  - F. For control of ventricular arrhythmias associated with cardiac glycoside (e.g., digitalis) toxicity; or
  - G. For treatment of plutonium, americium, and curium overload secondary to environmental or working conditions.
  
- II. It is the policy of Health Net of California that chelation therapy is considered investigational for, but not limited to, any of the following scenarios since there is inadequate scientific evidence in the peer-reviewed medical literature to support its efficacy:
  - A. For cardiovascular or coronary heart disease; or
  - B. Neurodegenerative diseases such as Alzheimer's disease; or
  - C. Any type of cancer including glioblastoma; or
  - D. Parkinson's disease; or
  - E. Autism; or
  - F. Multiple sclerosis



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**III.** It is the policy of Health Net of California that chelation therapy is considered not medically necessary for, but not limited to, any of the following scenarios since there is inadequate scientific evidence in the peer-reviewed medical literature to support its efficacy:

- A. Atherosclerosis; or
- B. Reperfusion injury during cardiopulmonary bypass surgery; or
- C. Hypercholesterolemia; or
- D. Scleroderma; or
- E. Treatment of renal calculi; or
- F. Porphyria; or
- G. Ankylosing spondylitis; or
- H. Peripheral vascular disease; or
- I. To prevent or reduce anthracycline-associated cardiac damage in women with breast cancer; or
- J. Rheumatoid arthritis.

### Background

Chelation therapy is an established treatment for treating heavy metal toxicities. It involves the administration of intravenous, intramuscular or oral chelating agents designed to convert such heavy metal ions such as lead, aluminum, mercury, arsenic, zinc, iron, copper, and calcium into inert forms so that they may be excreted. Chelation therapy has been proposed to treat metal toxicity from dental amalgam fillings, but it has not been shown that mercury amalgams cause harm to patients with dental fillings, except in rare cases of allergy.

Chelation therapy may be indicated for treatment of lead overload in children with blood lead levels > 45 µg/dL. Significantly lower levels of 30 mcg/dL in children can cause mental retardation or cognitive and behavioral problems. A complete blood count is also done to check for abnormalities on red blood cells (basophilic stippling). In children, long-bone x-rays may reveal bands called "lead lines" that indicate failure of the bone to rebuild. These bands are not actual lead concentrations, but are bone abnormalities. Symptoms in adults may not appear until blood lead levels exceed 80mcg/dL.

Chelation therapy may be indicated for treatment of mercury overload. A 24-hour urine specimen is collected for measurement of mercury levels. Chest x-rays can reveal a collection of mercury from exposure to elemental mercury or a pulmonary embolism containing mercury. Abdominal x-rays can reveal swallowed mercury as it moves through the gastrointestinal tract. Blood and urine samples are used to determine recent exposure, as well as exposure to elemental mercury and inorganic forms of mercury. Scalp hair is used in testing for exposure to methylmercury. Blood mercury levels should not exceed 50 mcg/L.

Chelation therapy may also be used for arsenic. Arsenic levels can be measured in blood, urine, hair, and fingernails. Because arsenic clears fairly rapidly from the blood, blood tests are not



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always useful. Therefore, urine tests are the most reliable for arsenic exposure within the past few days; hair and fingernail testing are used to measure exposure over the past several months.

Chelation may also be indicated for elevated levels of cadmium, where blood levels of cadmium above 5 mcg/dL suggest cadmium toxicity and for elevated level of aluminum. Levels of aluminum that are recognized as average are less than 0.01 mg/L. However, blood testing might underestimate the total body level of aluminum; postmortem brain, lung, and bone measurements reveal much higher levels of aluminum than blood tests.

Chelating agents are potentially toxic and should not be used unless absolutely indicated. These agents, especially those intended for use in children, should be effective in reducing lead and other heavy metals from the body without producing substantial adverse effects on levels of critical serum electrolytes, such as calcium. The only agent recommended for intravenous (IV) chelation therapy for children is CaEDTA. According to the FDA and the CDC, the safety and effectiveness of Na<sub>2</sub>EDTA in pediatric patients has not been established, and its use is not recommended because it induces hypocalcemia and possibly fatal tetany.

#### Non-overload Conditions

Chelation therapy has been investigated as a treatment for a variety of non-overload conditions, such as atherosclerosis, anthracycline-associated heart damage, coronary heart disease, peripheral vascular disease, various forms of cancer, Alzheimer's disease, rheumatoid arthritis, and countless other diagnoses. Chelation therapy is not FDA approved for any of these scenarios.

The proposed benefits of chelation therapy for non-overload conditions include increased collateral blood circulation; decreased blood viscosity; improved cell membrane function; improved intracellular organelle function; decreased arterial vasospasm; decreased free radical formation; inhibition of the aging process; reversal of atherosclerosis; decrease in angina; reversal of gangrene; improvement of skin color, healing of diabetic ulcers. Proponents also claim that chelation is effective against arthritis; multiple sclerosis; Parkinson's disease; psoriasis; Alzheimer's disease; and problems with vision, hearing, smell, muscle coordination, and sexual potency. None of these claimed benefits have been demonstrated by well-designed clinical trials.

The American Heart Association (AHA), The U.S. Food and Drug Administration (FDA), National Institutes of Health (NIH), and the American College of Cardiology (ACC) (2008) state that there is no scientific evidence to demonstrate any benefit from chelation therapy with ethylenediamine tetraacetic acid (E.D.T.A.), to treat arteriosclerotic heart disease.

The American Medical Association (AMA) (2007) state that there is no scientific documentation that the use of chelation therapy is effective in the treatment of cardiovascular disease, atherosclerosis, rheumatoid arthritis, and cancer. If chelation therapy "is to be considered a useful medical treatment for anything other than heavy metal poisoning, hypercalcemia or digitalis toxicity, it is the responsibility of its proponents to conduct properly controlled scientific



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studies, to adhere to FDA guidelines for drug investigation, and to disseminate study results in the usually accepted channels.”

### Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2015, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

CPT® Codes	Description
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)
96367	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); additional sequential infusion, up to 1 hour (List separately in addition to code for primary procedure)

HCPCS Codes	Description
J0470	Injection, dimercaprol, per 100 mg
J0600	Injection, edetate calcium disodium up to 1,000 mg
J0470	Injection, dimercaprol, per 100 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, care coordination, and all necessary supplies and equipment, per diem

### ICD-10-CM Diagnosis Codes

ICD-10-CM Code	Description
D50.0-D50.9	Iron deficiency anemia
D56.0-D56.9	Thalassemias



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ICD-10-CM Code	Description
D57.00-D57.89	Sickle-cell disorders
D61.01-D61.9	Other aplastic anemias and other bone marrow failure syndromes
D64.1-D64.3	Hereditary secondary sideroblastic anemia due to disease or drugs and toxins
E80.0-E80.29	Hereditary erythropoietic porphyria, unspecified and other porphyria
E83.00-E83.19	Disorders of mineral metabolism
E83.52	Hypercalcemia
F84.0	Autistic disorder
G20	Parkinson's disorder
G35	Multiple sclerosis
I01.0-I01.9	Rheumatic fever with heart involvement
I10-I15.9	Hypertensive disease
I26.0-I28.9	Pulmonary heart disease and diseases of pulmonary circulation
I30.0-I52	Other forms of heart disease
I70.201-I70.299	Atherosclerosis of native arteries of the extremities
I70.301-I70.92	Atherosclerosis of unspecified type of bypass graft(s) of the extremities
I73.9	Peripheral vascular disease, unspecified
K74.3-K74.5	Biliary cirrhosis
L11.0	Acquired keratosis follicularis
L94.0	Localized scleroderma (morphea)
M45.0-M45.9	Ankylosing spondylitis
N18.6	End stage renal disease
N20.0	Calculus of kidney
N25.8-N25.89	Other disorders resulting from impaired renal tubular function
R53.86	Other fatigue
T37.8X1-T37.8X6	Poisoning by, adverse effects of and underdosing of other specified systemic anti-infectives and antiparasitics
T39.4X1-T39.4X6	Poisoning by, adverse effects of and underdosing of other specified systemic anti-infectives and antiparasitics
T45.4X1-T45.4X6	Poisoning by, adverse effects of and underdosing of iron and its compounds
T56.0X1-T56.94	Toxic effect of metals
Z77.011	Contact with and (suspected) exposure to lead

Reviews, Revisions, and Approvals	Date	Approval Date
Initial policy	03/08	04/08
Code updates		12/13



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Reviews, Revisions, and Approvals	Date	Approval Date
Added superconducting quantum interference device (SQUID) for the measurement of hepatic iron concentration when there is chronic iron overload, as investigational. Code updates	10/13	10/13
Codes updated	10/14	10/14
No changes	10/15	10/15
Revised to Centene format. SQUID removed	10/16	10/16
No changes	10/17	10/17
Updated codes and references.	10/18	10/18
Minor wording changes, updated references, pharmacy policies related to chelating agents for iron overload are available	10/19	10/19

**References**

1. American College of Cardiology. Position Statement on Chelation Therapy. 2/26/2016
2. Fihn SD, Blankenship JC, Alexander KP, et al. 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* 2014;64:1929–49.
3. Ambati SR, Randolph RE, Mennitt K, et al. Longitudinal monitoring of cardiac siderosis using cardiovascular magnetic resonance T2\* in patients with thalassemia major on various chelation regimens: a 6-year study. *Am J Hematol*. 2013 Aug;88(8):652-6.
4. Antoniades V, Sioga A, Dietrich EM, et al. Is copper chelation an effective anti-angiogenic strategy for cancer treatment? *Med Hypotheses*. 2013 Oct 11.
5. Bedford MR, Ford SJ, Horniblow RD, et al. Iron chelation in the treatment of cancer: a new role for deferasirox? *J Clin Pharmacol*. 2013 Sep;53(9):885-91.
6. Born T, Kontoghiorghis CN, Spyrou A, et al. EDTA chelation reappraisal following new clinical trials and regular use in millions of patients: review of preliminary findings and risk/benefit assessment. *Toxicol Mech Methods*. 2013 Jan;23(1):11-7.
7. Breccia M, Finsinger P, Loglisci G, et al. Deferasirox treatment for myelodysplastic syndromes: "real-life" efficacy and safety in a single-institution patient population. *Ann Hematol*. 2012 Sep;91(9):1345-9.
8. Cassinerio E, Roghi A, Pedrotti P, et al. Cardiac iron removal and functional cardiac improvement by different iron chelation regimens in thalassemia major patients. *Ann Hematol*. 2012 Sep;91(9):1443-9.
9. Delforge M, Selleslag D, Beguin Y, et al. Adequate iron chelation therapy for at least six months improves survival in transfusion-dependent patients with lower risk myelodysplastic syndromes. *Leuk Res*. 2014;38(5):557-563.
10. Devos D, Moreau C, Devedjian JC, et al. Targeting chelatable iron as a therapeutic modality in Parkinson's disease. *Antioxid Redox Signal*. 2014; 21(2):195-210.



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11. 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*. 2014;7(1):15-24.
12. Gattermann N, Finelli C, Della Porta M, et al. Hematologic responses to deferasirox therapy in transfusion-dependent patients with myelodysplastic syndromes. *Haematologica*. 2012 Sep;97(9):1364-71.
13. Hamidieh AA, Moeininia F, Tayebi S, et al. Efficacy of hepatic T2\* MRI values and serum ferritin concentration in predicting thalassemia major classification for hematopoietic stem cell transplantation. *Pediatr Transplant* 2015; 19:301.
14. Hernando D, Levin YS, Sirlin CB, et al. Quantification of Liver Iron with MRI: State of the Art and Remaining Challenges. *J Magn Reson Imaging*. 2014 Nov; 40(5): 1003–1021. 2014 Mar 3.
15. Hoffman: *Hematology: Basic Principles and Practice*, 6th ed. Assessment of Iron Stores. 2012 Saunders, An Imprint of Elsevier.
16. Ktena YP, Athanasiadou A, Lambrou G, et al. Iron chelation with deferasirox for the treatment of secondary hemosiderosis in pediatric oncology patients: a single-center experience. *J Pediatr Hematol Oncol*. 2013 Aug;35(6):447-50.
17. 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*. 2014; 168(1):37-44.
18. 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*. 2013 Mar 27;309(12):1241-50.
19. Lamas GA, Goertz C, Boineau R, et al. Design of the Trial to Assess Chelation Therapy (TACT). *Am Heart J*. 2012 Jan;163(1):7-12.
20. Maggio A, Filosa A, Vitrano A, et al. Iron chelation therapy in thalassemia major: a systematic review with meta-analyses of 1520 patients included on randomized clinical trials. *Blood Cells Mol Dis*. 2011 Oct 15;47(3):166-75.
21. Meerphol J, Schell L, Rucker G, et al. Deferasirox for managing iron overload in people with myelodysplastic syndrome. *Cochrane Database Syst Rev*. 2014a.
22. Nolte F, Höchsmann B, Giagounidis A, et al. Results from a 1-year, open-label, single arm, multi-center trial evaluating the efficacy and safety of oral Deferasirox in patients diagnosed with low and int-1 risk myelodysplastic syndrome (MDS) and transfusion-dependent iron overload. *Ann Hematol*. 2012 Oct 17.
23. Panch SR, Yau YY, West K, et al. Initial serum ferritin predicts number of therapeutic phlebotomies to iron depletion in secondary iron overload. *Transfusion* 2015; 55:611.
24. Remacha AF, Arrizabalaga B, Villegas A, et al. Evolution of iron overload in patients with low-risk myelodysplastic syndrome: Iron chelation therapy and organ complications. *Ann Hematol*. 2014 Dec 18 [Epub ahead of print].
25. Ruivard M. Iron chelating therapy in adults: How and when ? *Rev Med Interne*. 2012 Nov 26.
26. Sampson EL, Jenagaratnam L, McShane R. Metal protein attenuating compounds for the treatment of Alzheimer's disease. *Cochrane Database Syst Rev*. 2014.



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27. Schirer SL, Bacon BR. Chelation therapy for iron overload states. UpToDate. August 7, 2014. Updated September 2, 2015.
28. Schrier SL, Bacon BR. Pathophysiology and diagnosis of iron overload syndromes. UpToDate. August 26, 2014.
29. Schrier, SL et al Iron Chelators: choice of agent, dosing and adverse effect. UpToDate. October 2018
30. Schrier, SL et al Approach to the Patient with Iron Overload. UpToDate. June 2018
31. Taher AT, Porter J, Viprakasit V, et al. Deferasirox reduces iron overload significantly in nontransfusion-dependent thalassemia: 1-year results from a prospective, randomized, double-blind, placebo-controlled study. *Blood*. 2012 Aug 2;120(5):970-7.
32. Viprakasit V, Gattermann N, Lee JW, et al. Geographical variations in current clinical practice on transfusions and iron chelation therapy across various transfusion-dependent anaemias. *Blood Transfus*. 2012 Jul 12:1-14.
33. Weinreb O, Mandel S, Youdim MB, Amit T. Targeting dysregulation of brain iron homeostasis in Parkinson's disease by iron chelators. *Free Radic Biol Med*. 2013 Sep;62:52-64.
34. Yawn BP, Buchanan GR, Afenyi-Annan AN, et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members. *JAMA*. 2014; 312(10):1033-1048.
35. Zanella SG, di Sarsina PR. Personalization of multiple sclerosis treatments: using the chelation therapy approach. *Explore (NY)*. 2013 Jul-Aug;9(4):244-8.
36. Ilas SK, Zeidan AM, Duong V et al. The effect of iron chelation therapy on overall survival in sickle cell disease and  $\beta$ -thalassemia: A systematic review. *Am J Hematol*. 2018; 93(7):943-952.
37. Bacon BR. Iron Chelators,: Choice of agent, dosing, and adverse effects UpToDate. September 2019

### **Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

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**Note: For Medicare members,** to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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