Medical Policy

Subject:	Chelation Therapy		
Document #:	MED.00127	**Publish Date:**	07/07/2021
Status:	Reviewed	**Last Review Date:**	05/13/2021

Description/Scope

This document addresses the uses of chelation therapy. Chelation therapy uses naturally occurring or chemically designed molecules to reduce potentially dangerous levels of heavy metals within the body. Chelation therapy is routinely performed for cases of iron overload, lead poisoning, copper toxicity, and other heavy metal conditions. This document is not applicable to agents used for the treatment of drug overdose or toxicities.

Position Statement

Medically Necessary:

The administration of U.S. Food and Drug Administration (FDA) approved chelating agents is considered **medically necessary** treatment for individuals with relevant clinical findings suggestive of heavy metal toxicity and a probable exposure history in **any** of the following conditions when confirmed by laboratory testing*:

1. Individuals with disorders of iron metabolism (for example, primary or secondary hemochromatosis); **or**
2. Lead overload in cases of acute or long-term lead exposure; **or**
3. Individuals with disorders of copper metabolism (for example, Wilson's disease); **or**
4. Arsenic, mercury, iron, copper or gold poisoning when long-term exposure and toxicity has been confirmed; **or**
5. Aluminum overload in individuals on chronic hemodialysis.

***Note:** Laboratory testing to confirm heavy metal toxicity should include blood or plasma specimens. In the case of suspected arsenic or mercury toxicity, it may be more appropriate to confirm diagnosis through a non-challenged urinalysis.

Investigational and Not Medically Necessary:

Chelation therapy is considered **investigational and not medically necessary** for the treatment of all other conditions, including but not limited to:

1. Heavy metal toxicity diagnosed via provoked urine testing;
2. Alzheimer's disease;
3. Autism Spectrum Disorders (ASD);
4. Cadmium exposure;
5. Cardiovascular disease (prevention and treatment);
6. Chronic fatigue syndrome;
7. Symptoms thought to be secondary to dental amalgam therapy;
8. Parkinson's disease;
9. Peripheral vascular disease;
10. Rheumatoid arthritis.

Rationale

Chelation therapy can provide substantial clinical benefit for conditions where heavy metal overload has been accurately diagnosed. The diagnostic workup must consider the individual's history, an appropriate choice of testing methods, and the use of accurate and specific reference values. With specific regard to urine testing, the diagnosis and use of chelation therapy should not be performed based on post-challenge urine testing. In post-challenge or post-provoked urine testing, the individual is first given a chelating agent followed by urine testing for heavy metals. The American College of Medical Toxicology (ACMT), in their 2009 position statement on the use of "Post-Chelator Challenge Metal Urine Testing," states that "Scientific investigation to date has failed to establish a valid correlation between prior metal exposure and post-challenge test values" and that post-challenge urine testing is being conducted without needed reference values. The ACMT further states the following:

> It is therefore, the position of the American College of Medical Toxicology that post-challenge urinary metal testing has not been scientifically validated, has no demonstrated benefit, and may be harmful when applied in the assessment and treatment of patients in whom there is concern for metal poisoning.

With appropriate heavy metal toxicity diagnosis, several studies published in the peer-reviewed medical literature have established that chelation therapy can be useful in binding toxic metal ions and facilitating their excretion through the liver or kidneys, and mitigating the morbidity associated with heavy metal toxicity such as end organ damage and impaired neurologic functioning.

Although chelation therapy has been investigated as a treatment of a wide variety of diseases and conditions, including Alzheimer's disease, Parkinson's, autism spectrum disorders, and rheumatoid arthritis, there has not been adequate scientific evidence to prove the clinical utility of such methods. A meta-analysis by Ng and colleagues (2007) evaluated chronic mercury exposure in children and adolescents. The authors concluded that there was "no evidence to support the association between mercury poisoning and autism" and "there is a lack of data in the literature about the effect of chelation therapy in children with neuro-developmental disabilities." Further study is needed to ascertain the causal role of heavy metal overload in these conditions, followed by studies demonstrating the clinical benefit of chelation therapy.

Dental amalgams have been investigated as a cause of increased blood levels of mercury, potentially associated with a number of diseases and disorders such as chronic fatigue syndrome and Alzheimer's disease. In 2009, the American Dental Association's (ADA) Council on Scientific Affairs reviewed the scientific literature on amalgam and stated: "The scientific evidence supports the position that amalgam is a valuable, viable and safe choice for dental patients." The Journal of the American Dental Association (JADA) reported that researchers found "no significant association of Alzheimer's Disease with the number, surface area or history of having dental amalgam restorations" and "no statistically significant differences in brain mercury levels between subjects with Alzheimer's disease and control subjects." The ADA's position has been reaffirmed by the U.S. FDA Center for Devices and Radiological Health in 2002, 2006 and 2009. The ADA's 2010 amalgam safety update cites that "studies continue to support the position that dental amalgam is a safe restorative option for both children and adults."

Chelation therapy has been proposed as a treatment of coronary artery disease (CAD), based in part on the hypothesis that chelation could remove atherosclerotic calcium deposits or provide an antioxidant benefit. One small placebo-controlled randomized study of 84 individuals with atherosclerotic heart disease did not report any

advantage of chelation therapy, as measured by time to ischemia, at 27 weeks of follow-up (Anderson, 2003; Knudtson, 2002). The use of chelation therapy in lieu of established therapies, the lack of adequate prior research to verify its effectiveness and clinical utility, and the overall impact of CAD prompted the National Center for Complementary and Alternative Medicine (NCCAM) and the National Heart, Lung, and Blood Institute (NHLBI) to sponsor a large-scale clinical study. The 5-year Trial to Assess Chelation Therapy (TACT) in CAD began recruiting individuals in March of 2003. This multicenter, randomized, double-blind study enrolled more than 1600 participants aged 50 or older who had a history of heart attack. The study tested whether chelation therapy or high-dose vitamin therapy are effective for the treatment of CAD. The primary study endpoint of this trial was a composite of heart attack, stroke, hospitalization for angina, coronary revascularization, and death. The study also evaluated cardiac deaths, nonfatal heart attacks, health-related quality of life (HR-QOL), and cost effectiveness, among other factors. Final results indicated that among stable individuals with a history of heart attack, an intravenous chelation regimen with disodium ethylenediaminetetraacetic acid (EDTA), when compared with placebo, modestly reduced the risk of negative cardiovascular outcomes, particularly revascularization procedures. Study authors emphasized that these results are insufficient to support the routine use of chelation therapy for treatment of individuals who have previously suffered from a heart attack (Lamas, 2013; Lamas, 2014; Escolar, 2014).

Background/Overview

Chelation therapy involves the administration of drugs that bind heavy metal ions such as lead, arsenic, iron, and mercury in the blood stream preventing their interaction with vital organs, such as the brain and kidneys. Drugs used in the administration of chelation therapy are known as chelating agents. The presence of heavy metals in the blood stream can be the result of several environmental exposures, including intake in water and food or in some instances such as lead, inhaling the metal from the air in a location where it is in excess. One common cause of lead exposure is through older buildings (built before 1978) in which lead based paints were used. There are occupational settings where high levels of metals can occur as well. Additionally, certain medical conditions lead to excess iron in the blood that may cause health problems. Chelation therapy reduces the accumulation of essential heavy metals, such as iron and copper or nonessential metals, such as lead and aluminum. Chelators bind with heavy metal ions and enhance the urinary and fecal excretion of these toxic metals. Specific chelating agents are used to bind specific heavy metals.

Chelation therapy has been proposed as a treatment for the removal of heavy metal ions to reduce cellular oxidative damage caused by the production of hydroxyl radicals. This therapy is under investigation for the treatment of numerous non-overload conditions including, but not limited to, cardiovascular disease, reperfusion injury during coronary angioplasty or cardiopulmonary bypass surgery, anthracycline-associated cardiac damage, Alzheimer's disease, Parkinson's disease, autism spectrum disorders (ASD), and rheumatoid arthritis.

Chelation agents, however, also have potential toxicity. Chelation agents have been known to bind elements in the body which are necessary for regular functioning, including zinc and calcium. Large doses of vitamins usually accompany the use of chelation agents to lessen these types of side effects. When there is life threatening heavy metal toxicity necessitating treatment with high doses of chelating agents, treatment in the hospital may be needed to monitor for possible side effects. Under less urgent circumstances, chelating agents may be administered on an outpatient basis.

Definitions

Autism Spectrum Disorder (ASD): A collection of associated developmental disorders that affect the parts of the brain associated with social interaction and verbal and non-verbal communication.

Primary hemochromatosis: A rare genetic disease that results in the overabundance of iron in the liver, brain, heart and kidneys, causing liver dysfunction, diabetes, changes in skin pigmentation, heart problems, arthritis and testicular atrophy.

Secondary hemochromatosis: A type of hemochromatosis which is usually the result of another condition or disease that causes the overabundance of iron. This disease and condition may include anemias, chronic liver diseases, and the requirement of blood transfusions.

Sickle cell disease: An inherited genetic disorder that causes red blood cells to take on a characteristic crescent or sickle-like shape with decreased ability to carry oxygen.

Sideroblastic anemia: A condition in which there is excess iron in the bone cells.

Thalassemia intermedia: A genetic form of anemia in which there is an abnormality in the oxygen carrying portion of red blood cells.

Wilson's disease: An inherited (autosomal recessive) disorder where excessive quantities of copper build up in the body, particularly in the liver and central nervous system.

Coding

The following codes for treatments and procedures applicable to this document 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 policy. 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.

When services may be Medically Necessary when criteria are met:

HCPCS	
J0470	Injection, dimercaprol, per 100 mg [BAL in oil]
J0600	Injection, edetate calcium disodium up to 1,000 mg
J0895	Injection, deferoxamine mesylate, 500 mg [Desferal]
J3520	Edetate disodium, per 150 mg
M0300	IV chelation therapy
S9355	Home infusion therapy, chelation therapy; administrative services, care coordination, and all necessary supplies and equipment, per diem

ICD-10 Diagnosis	
D56.0-D56.9	Thalassemia
D57.00-D57.819	Sickle-cell disorders
D61.01-D61.9	Other aplastic anemias and other bone marrow failure syndromes

D64.0-D64.3	Sideroblastic anemias (hereditary, secondary, other)
E83.00-E83.09	Disorders of copper metabolism [includes Wilson's disease]
E83.10-E83.19	Disorders of iron metabolism [includes hemochromatosis]
N18.6	End stage renal disease
T45.4X1S	Poisoning by iron and its compounds, accidental (unintentional); sequela
T45.4X2S	Poisoning by iron and its compounds, intentional self-harm; sequela
T45.4X3S	Poisoning by iron and its compounds, assault; sequela
T45.4X4S	Poisoning by iron and its compounds, undetermined; sequela
T45.4X5S	Adverse effect of iron and its compounds, sequela
T56.0X1A-T56.0X4S	Toxic effect of lead and its compounds
T56.1X1S	Toxic effect of mercury and its compounds, accidental (unintentional); sequela
T56.1X2S	Toxic effect of mercury and its compounds, intentional self-harm; sequela
T56.1X3S	Toxic effect of mercury and its compounds, assault; sequela
T56.1X4S	Toxic effect of mercury and its compounds, undetermined; sequela
T56.4X1S	Toxic effect of copper and its compounds, accidental (unintentional); sequela
T56.4X2S	Toxic effect of copper and its compounds, intentional self-harm; sequela
T56.4X3S	Toxic effect of copper and its compounds, assault; sequela
T56.4X4S	Toxic effect of copper and its compounds, undetermined; sequela
T56.891S	Toxic effect of other metals, accidental (unintentional); sequela [gold]
T56.892S	Toxic effect of other metals, intentional self-harm; sequela [gold]
T56.893S	Toxic effect of other metals, assault; sequela [gold]
T56.894S	Toxic effect of other metals, undetermined; sequela [gold]
T57.0X1S	Toxic effect of arsenic and its compounds, accidental (unintentional); sequela
T57.0X2S	Toxic effect of arsenic and its compounds, intentional self-harm; sequela
T57.0X3S	Toxic effect of arsenic and its compounds, assault; sequela
T57.0X4S	Toxic effect of arsenic and its compounds, undetermined; sequela
Z77.010	Contact with and (suspected) exposure to arsenic
Z77.011	Contact with and (suspected) exposure to lead
Z99.2	Dependence on renal dialysis

When services are Investigational and Not Medically Necessary:
For the procedure and diagnosis codes listed above when criteria are not met or for all other diagnoses not listed; or when the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

References

Peer Reviewed Publications:

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Dimercaprol
DMSA
Edathamil calcium disodium
Edathamil disodium
Edetate calcium disodium

Hemochromatosis
Pervasive Development Disorders
Sodium calcium EDTA
Wilson's Disease

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Document History

Status	Date	Action
Reviewed	05/13/2021	Medical Policy & Technology Assessment Committee (MPTAC) review. Updated References and Websites sections.
Reviewed	05/14/2020	MPTAC review. Updated References and Websites sections.
Reviewed	06/06/2019	MPTAC review. Updated References and Websites sections.
	04/24/2019	Changed the document number from DRUG.00003 to MED.00127 with same title.
Revised	07/26/2018	MPTAC review. Added confirmed laboratory testing to MN criteria. Updated Rationale, Background/Overview, Coding, and References sections.
Revised	03/22/2018	MPTAC review. Updated header language from "Current Effective Date" to "Publish Date." Removed non-specific diagnostic criteria from the MN statement. Updated References section.
Revised	05/04/2017	MPTAC review. Revised INV/NMN to DSM-5 language for ASD. Updated Rationale, Background/Overview, Definitions and References sections.
Revised	05/05/2016	MPTAC review. Fixed typo in position statement. Updated Reference section. Removed ICD-9 codes from Coding section.
Reviewed	05/07/2015	MPTAC review. Updated Description/Scope, Rationale, Background/Overview and Reference sections.
	01/01/2015	Updated Coding section with additional anemia diagnosis codes.
Reviewed	05/15/2014	MPTAC review. Updated Rationale, Coding and Reference sections.
Revised	05/09/2013	MPTAC review. Removed emergency treatment of hypercalcemia from Position Statement. Updated Coding section and Index.
Revised	02/14/2013	MPTAC review. Clarification to Position Statement about urine tests. Addition of autism and PDD to Investigational and Not Medically Necessary Position Statement. Updated Rationale, Background/Overview, References and Index.
Reviewed	02/16/2012	MPTAC review. Rationale, References, and Index updated.
	10/01/2011	Updated Coding section with 10/01/2011 ICD-9 changes.
Reviewed	02/17/2011	MPTAC review. Updated Rationale and References.
	10/01/2010	Updated Coding section with 10/01/2010 ICD-9 changes.
Revised	02/25/2010	MPTAC review. Clarification of medical necessity statement from "Patients with hemochromatosis who are not able to tolerate frequent phlebotomy" and "Secondary hemochromatosis due to chronic iron overload due to transfusion-dependent anemias (e.g., thalassemias, Cooley's anemia, sickle cell anemia, sideroblastic anemia)" to read "Individuals with disorders of iron metabolism (e.g., primary or secondary hemochromatosis)". "Copper overload in patients

		with Wilson's disease, a rare, hereditary condition" clarified to read "Individuals with disorders of copper metabolism (e.g., Wilson's disease)." Updated Background/Overview, Coding, References, Web Sites, Index.
Reviewed	05/21/2009	MPTAC review. Updated Rationale, References and Web Sites.
Reviewed	05/15/2008	MPTAC review. Updated Rationale, References, and Web Sites.
	02/21/2008	The phrase "investigational/not medically necessary" was clarified to read "investigational and not medically necessary." This change was approved at the November 29, 2007 MPTAC meeting.
Reviewed	05/17/2007	MPTAC review. Clarified Description. Updated Rationale, References, Web Sites and Coding.
Reviewed	06/08/2006	MPTAC review. References updated. No change in position.
	11/18/2005	Added reference for Centers for Medicare and Medicaid Services (CMS) – National Coverage Determination (NCD).
Revised	07/14/2005	MPTAC review. Revision based on Pre-merger Anthem and Pre-merger WellPoint Harmonization.

Pre-Merger Organizations	**Last Review Date**	**Document Number**	**Title**
Anthem, Inc.	07/27/2004	DRUG.00003	Chelation Therapy
WellPoint Health Networks, Inc.	06/24/2004	8.01.05	Chelation Therapy