BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Chelation Therapy

Policy #: 085
Category: Pharmacology

Latest Review Date: February 2020
Policy Grade: A

BACKGROUND:

Blue Advantage *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*
   - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
   - *Furnished in a setting appropriate to the patient's medical needs and condition;*
   - *Ordered and furnished by qualified personnel;*
   - *One that meets, but does not exceed, the patient's medical need; and*
   - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare* *for covered services that are related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

POLICY:

Effective for dates of service on or after November 3, 2013:

Blue Advantage will treat **chelation therapy** as a **covered benefit** in the treatment of **each** of the following conditions **when performed in the in-patient setting**:

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

Blue Advantage will treat **chelation therapy for the treatment of sickle cell anemia thalassemias and iron overload in patients requiring frequent transfusion** as a **covered benefit** when **taken orally** or **performed as an outpatient procedure or given in the home health setting.**

Blue Advantage will treat **chelation therapy in any form** (IV, PO, transdermal, topical or rectal) as a **non-covered benefit** when performed in an **in-patient or outpatient setting to treat any other condition**; including but not limited to, Alzheimer's disease, atherosclerosis, myocardial infarction, autism, and diabetes, and as **investigational**.

Blue Advantage any treatment associated with non-covered chelation therapy (e.g. glutathione and vitamin C) as a **non-covered benefit** and as **investigational.**

***Blue Advantage** will treat **chelation therapy performed to treat heavy metal and/or lead** poisoning detected by a **provocative urine** test as a non-covered benefit.

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

DESCRIPTION OF PROCEDURE OR SERVICE:

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

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

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

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

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

KEY POINTS:

This policy was updated with a literature search through December 9, 2019.

Summary

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

Practice Guidelines and Position Statements

American College of Physicians et al

In 2012, the American College of Physicians, American College of Cardiology Foundation, American Heart Association, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association and Society of Thoracic Surgeons published a clinical practice guideline on management of stable ischemic heart disease (IHD). The guidelines recommended that "chelation therapy should not be used with the intent of improving symptoms or reducing cardiovascular risk in patients with stable IHD. (Grade: strong recommendation; low-quality evidence)" However, citing the Trial to Assess Chelation Therapy, a 2014 focused update of this guideline included a revised recommendation on chelation therapy, stating that the "usefulness of chelation therapy is uncertain for reducing cardiovascular events in patients with stable IHD." The recommendation was upgraded from class III (no benefit) to class IIb (benefit ≥ risk), and the level of evidence from C (only consensus expert opinion, case studies, or standard of care) to B (data from a single randomized trial or nonrandomized studies).

In 2004, the ACP clinical practice guidelines stated that chelation "should not be used to prevent myocardial infarction or death or to reduce symptoms in patients with symptomatic chronic stable angina. (Level of evidence B: Based on evidence from a limited number of randomized trials with small numbers of patients, careful analyses of nonrandomized studies, or observational registries.)"

American College of Cardiology

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

Canadian Cardiovascular Society

Evidence-based, consensus guidelines from the Canadian Cardiovascular Society in 2014 included a conditional recommendation (based on moderate quality evidence) that chelation therapy should not be used to attempt to improve angina or exercise tolerance in patients with stable ischemic heart disease.

National Institute for Health and Care Excellence

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

U.S. Preventive Services Task Force Recommendations

Not applicable

KEY WORDS:
Chelation therapy, toxic metal ions, dimercaprol, edetate calcium disodium, deferoxamine, penicillamine, Succimer, Desferal

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

Several iron chelating agents have received FDA approval.

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

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

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

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

BENEFIT APPLICATION:
Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

CURRENT CODING:
HCPCS codes:

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

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This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield's administration of plans contracts.