Medical Coverage Policy | Chelation Therapy for Off-Label Uses

EFFECTIVE DATE: 01|01|2017
POLICY LAST UPDATED: 04|07|2021

OVERVIEW

Chelation therapy, an established treatment for heavy metal toxicities and transfusional hemosiderosis, has been investigated for a variety of off-label applications, such as treatment of atherosclerosis, Alzheimer disease, and autism. This policy addresses the following off-label uses of chelation therapy:

- Alzheimer disease
- Atherosclerotic cardiovascular disease
- Arthritis, including rheumatoid arthritis
- Autism spectrum disorder
- Diabetes
- Multiple sclerosis

This policy does not address the following U.S Food and Drug Administration (FDA)-approved indications for which chelation therapy is considered standard of care treatment:

- Extreme conditions of metal toxicity
- Treatment of chronic iron overload due to blood transfusions (transfusional hemosiderosis) or due to non-transfusion-dependent thalassemia (NTDT)
- Wilson disease (hepatolenticular degeneration)
- Lead poisoning
- Control of ventricular arrhythmias or heart block associated with digitalis toxicity
- Emergency treatment of hypercalcemia

This policy is applicable to Commercial Products only. For BlueCHiP for Medicare, see related policy section.

MEDICAL CRITERIA

Not applicable

PRIOR AUTHORIZATION

Not applicable

POLICY STATEMENT

Commercial Products

Off-label applications of chelation therapy (non-FDA-approved uses) are considered not medically necessary as the evidence is insufficient to determine that the technology results in an improvement in the net health outcome including, but no limited to:

- Alzheimer disease
- Arthritis (includes rheumatoid arthritis)
- Atherosclerosis (eg, coronary artery disease, secondary prevention in patients with myocardial infarction, or peripheral vascular disease)
- Autism
- Diabetes
- Multiple sclerosis

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage, or Subscriber Agreement for applicable not medically necessary benefits/coverage.

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 spectrum disorder. For example, EDTA chelation therapy has been proposed in patients with atherosclerosis as a method of decreasing obstruction in the arteries.

In 1953, 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 FDA for the treatment of lead poisoning in pediatric patients only. The FDA approved disodium-EDTA for use in selected patients with hypercalcemia and 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, which 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.

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 randomized controlled trials (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 (eg, high dropout rates) and, therefore, conclusions are not definitive. For other conditions, the available RCT's 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 that the technology results in an improvement in the net health outcome.

CODING

Commercial Products

The following code represents the infusion service only and is not separately reimbursed:

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.

Chemical Endarterectomy

The following code and any of the medications utilized as part of the service are not medically necessary when filed with the ICD-10 diagnosis codes below:

M0300 IV chelation therapy (chemical endarterectomy)

E08.00-E13.9 Diabetes mellitus code range
F84.0-F84.9 Autism spectrum disorders
G30.0-G30.9 Alzheimer's disease code range
G35 Multiple sclerosis
I25.10-I25.9 Atherosclerosis code range
M05.00-M06.09 Rheumatoid arthritis code range
M15.0-M19.93 Osteoarthritis code range

Failure of participating providers to report Chemical Endarterectomy using M0300 will be considered improper coding by BCBSRI.

RELATED POLICIES

BlueCHiP for Medicare National and Local Coverage Determinations Policy
Non-Reimbursable Health Service Codes

PUBLISHED

Provider Update, June 2021
Provider Update, September 2020
Provider Update, November 2019
Provider Update, November 2018
Provider Update, February 2018

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