BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Diagnosis and Treatment of Chronic Cerebrospinal Venous Insufficiency in Multiple Sclerosis

Policy #: 477
Latest Review Date: August 2022
Category: Medical

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:

Blue Advantage will treat the **identification and subsequent treatment of chronic cerebrospinal venous insufficiency (CCSVI) in patients with multiple sclerosis** as a **non-covered benefit** and as **investigational**.

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:

Chronic cerebrospinal venous insufficiency (CCSVI) may be associated with multiple sclerosis (MS), although this is controversial and an active area of research. Correction of CCSVI has been attempted via percutaneous venoplasty. The intent of this procedure is to relieve MS symptoms by improving venous drainage of the central nervous system.

The foundation of this vascular theory is that there is abnormal venous drainage from the brain due to outflow obstruction in the draining jugular vein and/or azygos veins. This abnormal venous drainage, which is identified by special ultrasound criteria, is said to cause intracerebral flow disturbance or outflow problems that lead to periventricular deposits. In the CCSVI theory, these deposits have a similarity to the iron deposits seen around the veins in the legs in individuals with chronic deep vein thrombosis. Those studying this theory have promoted the idea that balloon dilatation, with or without stenting, will resolve the CCSVI and alleviate MS complaints.

Multiple sclerosis (MS) is generally considered a chronic inflammatory demyelinating disease of the central nervous system (brain, spinal cord, optic nerve) felt to be triggered by an autoimmune response to myelin. However, in part due to the periventricular predilection of the lesions of multiple sclerosis, vascular etiologies (chronic cerebrospinal venous insufficiency [CCSVI]) have also been considered.

The following five criteria were defined by Zamboni et al as features of CCSVI. To make the diagnosis of CCSVI, at least two of the five criteria need to be present:

1. Reflux constantly present (for a duration >0.8 s) in the supine and upright positions at the level of an internal jugular or vertebral vein. This parameter was evaluated during a short breath-hold following normal breathing and not under Valsalva maneuver.
2. Reflux at the level of veins of the deep cerebral system (for a duration >0.5 s). This was evaluated with the patient in the sitting and supine positions, and venous flow was enhanced by inviting the patient to breath in.

3. Stenosis (<0.3 cm), valve abnormalities and septa on B-mode imaging.
4. Absence of flow at the level of the internal jugular or vertebral vein, despite numerous deep inspirations.
5. No increase in the diameter of the internal jugular vein when changing from an upright to a supine position (lack of change).

The association of CCSVI with MS is uncertain. The rate of CCSVI in MS patients varies widely in the literature for unclear reasons, from 0% to 100%. Some studies report higher rates of CCSVI in patients with MS compared with Non-MS patients, but others do not. If there is an association between MS and CCSVI, it is not known whether this is a causative factor for MS or a secondary result of the disease. It also appears that CCSVI can occur in other disorders and is not specific for MS.

Treatment of CCSVI with endovascular interventions has been attempted. Some currently available studies report improvement in patient-reported symptoms following treatment, but this evidence is not sufficient to establish efficacy. A prospective, double-blind, sham-controlled randomized controlled trial (RCT) of venous angioplasty in MS patients (N=20) with CCSVI published in 2014 showed no significant differences in venous outflow characteristics between the treated and control groups, nor any significant improvements in clinical disease scores among treated patients compared with controls. The results of three this RCT are limited by the small number of patients. However, the failure to show a beneficial effect of venous angioplasty on blood flow or symptoms supports a lack of efficacy for this treatment.

Adverse events occur at a low overall rate, but serious adverse events can occur, and the U.S. Food and Drug Administration (FDA) issued an alert in 2012 concerning the potential for serious adverse events with treatment of CCSVI.

KEY POINTS:

This policy is based on a literature search through August 9, 2022. The following is a summary of the key literature.

Summary of Evidence

For individuals who have multiple sclerosis who receive ultrasound with or without magnetic resonance imaging to diagnose CCSVI, the evidence includes systematic reviews and controlled observational studies. Relevant outcomes are test accuracy, test validity and other test performance measures. Systematic reviews have generally found a statistically significant association between CCSVI and MS when all studies are included but a 2014 meta-analysis that excluded studies by Zamboni (who proposed criteria for defining CCSVI) and associated research groups found no significant association. Moreover, systematic reviews have reported significant heterogeneity among studies. Recent observational studies have not found that Zamboni criteria or updated criteria proposed by the International Society for Neurovascular Disease (ISNVD) can discriminate between MS and Non-MS patients. The association between CCSVI and MS, especially as a causative factor, remains unclear. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have multiple sclerosis and CCSVI who receive percutaneous venoplasty, the evidence includes one RCT and several case series. Relevant outcomes are overall survival, symptoms, quality of life and treatment-related morbidity. The RCT was double blind and sham-controlled. It found no statistically significant differences in venous outflow characteristics or improvements in clinical disease scores between the groups treated with venoplasty versus a sham intervention. The small number of patients limits the results of this RCT and no other RCTs on the efficacy of percutaneous venoplasty were identified. Data on adverse events are available from the FDA and larger published case series (i.e., with several hundred patients). The case series found that adverse events were uncommon following venoplasty, but serious adverse events have been reported to the FDA. FDA issued an alert in May 2012, noting the existence of serious complications, including death, and the need for ongoing monitoring. It is not currently possible from the available literature to estimate the rate of serious adverse events such as death or major bleeding with confidence. The evidence is insufficient to determine the effects of the technology on health outcomes.

Practice Guidelines and Position Statements

International Society for Neurovascular Disease

In 2014, the International Society for Neurovascular Disease published a position statement on detection of extracranial venous abnormalities indicative of chronic cerebrospinal venous insufficiency (CCSVI). The document concluded:

"Although some CNS [central nervous system] disorders have been linked to the presence and severity of CCSVI, the ultimate cause-consequence relationship has not been firmly established. Therefore, it is not clear at this time which patient population should undergo the noninvasive and invasive studies for detection of extracranial venous abnormalities…."

Cardiovascular and Interventional Radiological Society

The Cardiovascular and Interventional Radiological Society of Europe (CIRSE) commentary on the treatment of chronic cerebrospinal venous insufficiency notes that:

"Thus far, no trial data are available, and there is currently no randomized controlled trial (RCT) in progress. Therefore, the basis for this new treatment rests on anecdotal evidence and successful testimonies by patients on the Internet. CIRSE believes that this is not a sound basis on which to offer a new treatment, which could have possible procedure-related complications, to an often desperate patient population."

The Society for Interventional Radiology (SIR)

The Society for Interventional Radiology (SIR) published a position statement on the association of CCSVI with MS and the efficacy of endovascular treatments. Their recommendations included the following statements:

- At present, SIR considers the published literature to be inconclusive on whether CCSVI is a clinically important factor in the development and/or progression of MS, and on whether balloon angioplasty and/or stent placement are clinically effective in patients with MS.

- SIR strongly supports the urgent performance of high-quality clinical research to determine the safety and efficacy of interventional MS therapies, and is actively working to promote and expedite the completion.

The U.K. National Institute for Health and Clinical Excellence (NICE)
The U.K. National Institute for Health and Clinical Excellence (NICE) published a guidance document on the use of percutaneous venoplasty to treat CCSVI in patients with MS. This document contained the following statements on the diagnosis and treatment of CCSVI:

- Current evidence on the efficacy of percutaneous venoplasty for chronic cerebrospinal venous insufficiency (CCSVI) for multiple sclerosis (MS) is inadequate in quality and quantity. Therefore, this procedure should only be used in the context of research.
- NICE encourages further research on percutaneous venoplasty for CCSVI for MS, in the form of robust controlled clinical trials. Studies should clearly define selection criteria and patient characteristics. They should also clearly define technical success, which may include measurement of pressure gradients across treated vein segments before and after venoplasty. Outcomes should include clinical and quality of life measures.

The European Society of Neurosonology and Cerebral Hemodynamics (ESNCH)
The European Society of Neurosonology and Cerebral Hemodynamics (ESNCH) issued a statement on CCSVI and MS in 2012. The ESNCH statement indicates the proposed criteria for the diagnosis of CCSVI is questionable due to methodological and technological errors, and lack of validation. The statement strongly discourages any interventional treatment for CCSVI in MS, such as transluminal angioplasty and/or stenting, due to lack of evidence and risk of serious complications.

U.S. Preventive Services Task Force Recommendations
Not applicable.

KEY WORDS:
Chronic cerebrospinal venous insufficiency, CCSVI, Liberation Procedure, CCSVI interventions, balloon venoplasty, catheter-based venoplasty, PTA of venous strictures in patients with CCSVI

APPROVED BY GOVERNING BODIES:
Endovascular correction of CCSVI is a surgical procedure and as such is not subject to FDA approval. However, in 2012, FDA issued an alert concerning the potential for serious adverse events with the treatment for CCSVI.

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

CURRENT CODING:

There is no specific code CPT for this test.

CPT Codes:

37248	Transluminal balloon angioplasty (except dialysis circuit), open or percutaneous, including all imaging and radiological supervision and interpretation necessary to perform the angioplasty within the same vein; initial vein
37249	Transluminal balloon angioplasty (except dialysis circuit), open or percutaneous, including all imaging and radiological supervision and interpretation necessary to perform the angioplasty within the same vein; each additional vein

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POLICY HISTORY:

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Medical Policy Group, November 2016
Medical Policy Group, October 2019
Medical Policy Group, August 2021
Medical Policy Group, August 2022: A peer-reviewed literature analysis was completed and no new information was identified that would alter the coverage statement of this policy.
