# FDA Safety Communication: Chronic Cerebrospinal Venous Insufficiency Treatment in Multiple Sclerosis Patients

U.S. Food & Drug Administration

**Date Issued:** May 10, 2012

**Audience:** People with multiple sclerosis (MS), their families and caregivers; Neurologists; Interventionalists (Radiologists, Vascular Surgeons and Neurosurgeons); Clinical Researchers; other MS health care providers; and Institutional Review Boards (IRBs).

**Medical Specialty:** Neurology, Interventional Radiology, Vascular Surgery.

**Purpose:** The FDA is alerting people with MS to the risks of serious injuries and death associated with procedures to treat chronic cerebrospinal venous insufficiency (CCSVI). Furthermore, the benefits of these experimental procedures have not been proven, and their promotion as a treatment for MS may lead people with the disease to make treatment decisions without being aware of the serious risks involved.

This communication is also intended to notify physicians and clinical investigators planning or conducting clinical trials using medical devices to treat CCSVI that they must comply with FDA regulations for investigational devices.

**Summary of Problem and Scope:** MS is a progressive, immune-mediated disorder of the brain and spinal cord. In this disorder, the lining around nerve fibers, and often the nerve fibers themselves, in the brain and spinal cord are injured, resulting in significant and disabling neurological symptoms.

The underlying cause of MS is not known. Some researchers think that narrowing (stenosis) of specific veins in the neck and chest (internal jugular and azygos veins) may cause MS or may contribute to the progression of MS by impairing blood drainage from the brain and upper spinal cord. This narrowing of neck and chest veins has been called CCSVI.

Studies exploring a link between MS and CCSVI are inconclusive. Some studies have suggested a link exists, while others have found no such connection. At this time, the FDA believes there is no reliable evidence from controlled clinical trials that this procedure is effective in treating MS. In addition, the criteria used to diagnose CCSVI have not been adequately established. Therefore, data to support CCSVI as a clinical entity on its own or its relationship with MS are inconclusive and at times, contradictory.

Some individuals, organizations and websites promote an experimental treatment

of CCSVI that uses balloon angioplasty devices or stents to widen the narrowed internal jugular or azygos veins. This procedure is sometimes called "liberation therapy" or the "liberation procedure".

The FDA believes that using these medical devices in CCSVI treatment procedures poses a risk to patients because:

- There is no clear diagnostic evidence that CCSVI exists as a distinct clinical disorder or is linked to MS.
- Venous stenoses seen on imaging tests may be normal variants that do not cause any symptoms or disease, since they are sometimes seen in healthy people.
- The safety and effectiveness of using balloon angioplasty devices or stents in the internal jugular or azygos veins have not been established for any clinical condition; nor has the FDA approved the use of these devices in these veins.
- There is no clear scientific evidence that the treatment of internal jugular or azygos venous stenosis is safe in MS patients, impacts the symptoms of MS, changes the overall course of MS or improves the quality of life for MS patients.
- It is possible that stent placement can worsen any venous narrowing. This is because further narrowing has been shown to sometimes occur within stents placed in veins, due to the body’s response to the implant.

The FDA encourages research to evaluate the relationship between CCSVI and MS and to characterize the safety and effectiveness of treatment procedures. Rigorously conducted, properly targeted research can provide a more complete understanding of the existence of CCSVI and any relationship between CCSVI and MS, which will help people with the disease and their clinicians make the best treatment decisions.

**Adverse Events:** CCSVI procedures have been associated with serious, even fatal, complications. The FDA has received reports of one patient who died from bleeding in the brain and one patient who suffered permanent paralysis from a stroke after CCSVI treatment. Other serious complications of the CCSVI procedure reported primarily as individual incidents or case series in medical journals include: at least one death, stents migrating from their original location to another part of the body (including the heart), venous injury, blood clots forming in the jugular vein or in stents, blood clots in a vein in the brain, cranial nerve damage, and abdominal bleeding. The frequency of these serious complications is not known.

**Recommendations:**

**For People with Multiple Sclerosis:**

- Be aware that there is lack of clear evidence of the existence of CCSVI. Furthermore, the link between CCSVI and MS and the safety and

effectiveness of the CCSVI treatment procedure in MS patients has not been established.
- You should know that serious complications can occur as a result of CCSVI treatment procedures. Before you have any CCSVI procedure, discuss with your physician or other health care provider the signs and symptoms of such complications. If you have the procedure and you develop any of the signs or symptoms of a complication, contact your health care provider immediately.
- Before considering CCSVI treatment, discuss the potential risks and benefits with a neurologist or other health care provider who is familiar with MS and CCSVI (including the CCSVI procedures and their outcomes).
- If you decide to undergo diagnostic and/or treatment procedures for CCSVI, continue to follow the MS treatment plan outlined by your neurologist or the provider caring for your MS.
- If you are considering participating in a clinical trial for CCSVI, learn as much as possible about the clinical trial and ask questions of the health care team conducting the trial. Read the informed consent document carefully, and ask for an explanation of anything you do not understand. You can find additional information and recommended questions to ask your health care team on the Understanding Clinical Trials page of www.clinicaltrials.gov [1].
- If you undergo treatment for CCSVI and experience a complication, we encourage you to file a report through MedWatch, the FDA Safety Information and Adverse Event Reporting program [2].

**For Physicians and Care Providers:**

- Inform patients of the following concerns:
    - there is conflicting evidence about CCSVI as a clinical entity;
    - CCSVI's relationship to MS is scientifically unproven; and
    - consensus on the diagnostic criteria of CCSVI has not been reached.
- You should be aware the FDA has not cleared or approved any angioplasty device or stents for the treatment of CCSVI and use of such devices in treating CCSVI are considered off-label at this time. While the FDA does not regulate the practice of medicine and health care practitioners may choose to use a legally marketed device, based on their clinical assessment, for purposes other than the cleared or approved use, the FDA believes the safety issues observed to date warrant a communication on the subject.
- Discuss the risks of CCSVI treatment with potential patients, including both the adverse events generally associated with catheter-guided endovascular intervention and those related specifically to use of balloon angioplasty devices or venous stenting for CCSVI.
- If your patient experiences a complication following CCSVI treatment, please file a report through MedWatch, the FDA Safety Information and Adverse Event Reporting program [3].

**For Clinical Investigators and Institutional Review Boards (IRBs):**

- The FDA has determined that investigations of medical devices for use in CCSVI treatment are significant risk studies. Clinical studies of significant risk medical devices, such as in the case of balloon angioplasty devices and stents to treat CCSVI, require approval through an IRB and the FDA's Investigational Device Exemption (IDE) program [4]. The IDE regulations help ensure the rights, safety and welfare of patients are protected during these studies and that the risks are as low as possible and are balanced by any potential benefits.
- The FDA encourages clinical investigators to discuss trial design with the FDA in the early planning phase, through both the formal pre-IDE process [5] and less formal meetings and conferences.
- If a patient in an IDE study experiences a complication related to the CCSVI treatment, sponsors and clinical investigators must comply with applicable adverse event recordkeeping and reporting requirements under the FDA's IDE regulations [6].

**FDA Activities:**

The FDA sent a warning letter [7] to a sponsor/investigator who was conducting a clinical study of CCSVI treatment without an approved IDE. Because the FDA currently considers clinical studies evaluating CCSVI treatment with balloon angioplasty devices and/or stents to be significant risk, this study was in violation of the FDA's regulations. The sponsor/investigator has reported the study has been voluntarily closed.

The FDA will continue to monitor for adverse events related to medical devices commonly used in CCSVI treatment (e.g. angioplasty devices and stents) and take action when appropriate.

The FDA will continue to monitor this situation and keep the public informed as new information becomes available.

**Contact Information:**
If you have questions about this communication, please contact the Division of Small Manufacturers, International and Consumer Assistance (DSMICA) at DSMICA@FDA.HHS.GOV [8], 800-638-2041 or 301-796-7100.

SOURCE [9]

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**Links:**
[1] http://www.clinicaltrials.gov/ct2/info/understand
[2] http://www.fda.gov/Safety/MedWatch/HowToReport/ucm053074.htm
[3] http://www.fda.gov/Safety/MedWatch/HowToReport/ucm085568.htm

[4] http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080202.htm
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