Update on Risk of Type III Endoleaks with Use of Endologix AFX Endovascular AAA Graft Systems: FDA Safety Communication

Date Issued: October 28, 2019

The FDA is evaluating new information about the risk of blood continuing to leak into the aneurysm (Type III endoleak) when Endologix AFX endovascular grafts (AFX with Strata, AFX with Duraply, or AFX2) are used for the treatment of abdominal aortic aneurysms (https://medlineplus.gov/ency/article/000162.htm) (AAA). We've previously communicated (/medical-devices/letters-health-care-providers/update-type-iii-endoleaks-associated-endovascular-graft-systems-letter-health-care-providers) about the greater risk of Type III endoleaks occurring with the Endologix AFX with Strata device compared to other endovascular graft systems, which can result in serious injury. It is important for patients and health care providers to be aware that data from an integrated healthcare system, published in a recent conference abstract, suggest there also may be a higher than expected risk of Type III endoleaks occurring with the use of AFX with Duraply and AFX2 endovascular grafts. We recommend lifelong follow-up for patients treated with any endovascular graft. However, while we continue our evaluation, we are emphasizing the importance of at least yearly, lifelong follow-up for all patients who have any type of Endologix AFX endovascular graft in order to monitor for Type III endoleaks.

Patients: Important Recommendations If You Have or Are Considering An Endologix AFX Endovascular Graft System for Treatment of Abdominal Aortic Aneurysm

- Be aware that the FDA has approved endovascular grafts made by various manufacturers for the treatment of AAA, and each device has specific benefits and risks.
- Prior to surgery, discuss the benefits and risks of all available AAA treatment options with your health care provider.
- If you have already had treatment of your AAA with an endovascular graft system, review the implant card that you received at the time your AAA was treated to determine if you have any type of Endologix AFX endovascular graft implanted. If you do not know if you have an AFX endovascular graft or if you do not have your implant card, please contact the health care provider who treated your AAA or the hospital where you were treated to find out.

- If you have any type of Endologix AFX endovascular graft, contact the health care provider who treated your AAA or another vascular specialist about further care and to discuss continued follow-up.
- Be aware that recent data suggest there may be a higher than expected risk of blood continuing to leak into the AAA (Type III endoleak) which can result in serious injury, including death when any AFX endovascular graft is used for the treatment of AAA.
    - As a result the FDA recommends at least yearly, lifelong follow-up for all patients who have had their AAA treated with any AFX endovascular graft system.
    - If you have an AFX endovascular graft and are overdue for a follow-up, make an appointment with the health care provider who treated your AAA or another vascular specialist to get your device checked.

Important Recommendations for Health Care Providers who treat and follow patients with an Endologix AFX Endovascular Graft System for Treatment of Abdominal Aortic Aneurysm:

- Prior to surgery, discuss the benefits and risks of all available AAA treatment options with your patients.
    - The benefit-risk profile of AFX endovascular grafts compared to alternative treatment options should be considered for each individual patient.
    - When making AAA treatment recommendations, and as part of the informed consent process, consider that recent data suggest there may be a higher than expected risk of Type III endoleaks in patients treated with any Endologix AFX endovascular grafts.
- Read and carefully follow the Endologix AFX Endovascular AAA System Instructions for Use (IFU), which was revised in 2018 (https://endologix.com/wp-content/uploads/2018/07/AFX-Safety-Update-AFX-Users_July2018.pdf) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) with updated information regarding Type III endoleaks.
    - The IFU includes component overlap recommendations, Type III endoleak risk factors and patient-tailored surveillance recommendations to assist health care providers in developing individualized patient follow-up plans.
- Closely monitor patients who have previously undergone implantation with any AFX endovascular graft and evaluate their risk profile for Type III endoleaks per the IFU.
    - Ensure yearly imaging follow-up at a minimum to monitor for the development of Type III endoleaks and aneurysm expansion for any patients under your care who

have previously undergone implantation with any AFX endovascular graft (AFX with Strata, AFX with Duraply, or AFX2)

- A benefit-risk determination for each individual patient should be considered to assess the need for additional procedures related to the risk of developing Type III endoleaks.

Device Description:

An endovascular graft can be used to treat an abdominal aortic aneurysm (https://medlineplus.gov/ency/article/000162.htm) (AAA). Endovascular grafts are flexible fabric tubes supported by a metal framework either on the inside or outside of the fabric. The endovascular graft is permanently implanted inside the largest blood vessel (aorta) so that blood flows through the endovascular graft instead of to the aneurysm, reducing the risk of further aneurysm growth or rupture. These devices are made by various manufacturers, and each of the devices used to treat AAAs has specific benefits and associated risks.

The AFX Endovascular AAA System (AFX), manufactured by Endologix, Inc., is an endovascular graft system intended to treat patients with AAA. The AFX endovascular graft was approved by the FDA in 2011 and over time, the manufacturer has made changes to the device resulting in the following versions of the device being implanted in patients:

- **AFX with Strata graft material,** which was implanted in patients between 2011 and 2016 but is no longer available on the market , after Endologix (https://endologix.com/wp-content/uploads/2016/12/12-30-Physician-Letter-AFX-TIII-Endoleak-FINAL.pdf) (http://www.fda.gov/about-fda/website-policies/website-disclaimer) requested that all AFX with Strata devices be removed from hospital inventory because of an increase in Type III endoleaks.
- **AFX with Duraply graft material,** which has been implanted in patients since July 2014 with the change in graft material from Strata to Duraply, which was intended to help prevent Type III endoleaks.
- **AFX2 (Duraply graft material),** which has been implanted in patients since February 2016 with changes to the manufacturing of the Duraply graft material to increase the average thickness and further help prevent Type III endoleaks.

In addition, the manufacturer over time has updated the instructions for use (IFU) for the device. The main change to address Type III endoleaks occurred in 2015, which included instructions regarding device sizing, as well as to increase the amount of overlap between graft segments that are joined together to treat the AAA.

Type III Endoleak

Various types of endoleaks can occur after repair with any endovascular graft and typically do not result in any symptoms. Therefore, patients who have been treated with **any** endovascular graft require regular, lifelong follow-up imaging (for example, a CT scan (/radiation-emitting-products/medical-x-ray-imaging/computed-tomography-ct)) for the detection of endoleaks.

Type III endoleaks in particular consist of blood flowing or leaking into the AAA either between endovascular graft segments that were joined together to treat the AAA at the time of implantation but have now separated (Type IIIa) or through holes in the graft material (Type IIIb). If left undetected and without treatment, a Type III endoleak may lead to expansion and rupture of the AAA. This may result in serious patient injury, including death. Imaging should be performed as part of the regular, lifelong follow-up, to determine if blood is continuing to flow through the endovascular graft device and not leaking into the AAA.

FDA Actions

AFX with Strata graft material

Patients previously treated for an AAA with the **AFX with Strata** endovascular graft are at greater risk for a Type III endoleak compared to other endovascular graft systems. As a result, Endologix has not manufactured the AFX with Strata graft material since July 2014 and health care providers were advised to remove any remaining inventory from shelves in December 2016 (https://endologix.com/wp-content/uploads/2016/12/12-30-Physician-Letter-AFX-TIII-Endoleak-FINAL.pdf) (http://www.fda.gov/about-fda/website-policies/website-disclaimer). Given the greater risk for Type III endoleaks occurring with the AFX with Strata endovascular graft, we continue to work collaboratively with Endologix to assess the Type III endoleak treatment options for patients who remain implanted with this specific device, and to provide further instructions in the labeling on this concern.

AFX with Duraply graft material or AFX2

We are evaluating recent real world data published in a recent conference abstract which suggest a higher than expected risk of Type III endoleaks occurring in patients treated for an AAA with an AFX endovascular graft with Duraply graft material **(AFX with Duraply or AFX2)**. The abstract presents prospective registry data from an integrated healthcare system that suggest an early Type III endoleak risk for all AFX endovascular grafts (AFX with Strata, AFX with Duraply and AFX2). According to the abstract, there was a 2.5% cumulative probability of additional procedures needed to treat Type III endoleaks at two years of follow-up for patients with AFX endovascular grafts (95% CI 1.5 to 4.2). The FDA recognizes the limitations of the data presented in the abstract, including the small number of patients with AFX2 (n=32 patients with AFX2; n=197 patients with AFX with Duraply; n=374 patients with AFX with Strata), the results not being stratified by Type IIIa and Type IIIb endoleak, and no comparison of the results to other endovascular graft systems. However, the abstract provides

published results from the largest US cohort of patients receiving Endologix AFX endovascular grafts.
We are also evaluating early postmarket data which compares the risk of Type III endoleaks with AFX endovascular grafts to other endovascular graft systems.

- The FDA has reviewed real world data from a vascular registry which suggest a significantly higher rate of Type III endoleaks for AFX with Strata and AFX with Duraply endovascular grafts as compared to the combined Type III endoleak rate for other endovascular grafts at one year of follow-up. The registry reports the Type III endoleak rate of AFX with Strata and AFX with Duraply together, so individual rates by graft material are not available. At this time, specific to AFX2, the data only include a small number of patients with follow-up (i.e., approximately 12% of AFX2 patients have follow-up data at one year) which does not allow for a meaningful interpretation.
- The FDA has reviewed data provided by Endologix from their ongoing clinical trial of AAA patients who randomly received either an AFX endovascular graft device with Duraply (AFX with Duraply or AFX2) or an FDA approved endovascular graft from other manufacturers. This study is called the LEOPARD Trial (Looking at EVAR Outcomes by Primary Analysis of Randomized Data). In contrast to the registry data, the most recent results indicate that the cumulative probability of Type III endoleaks is 1.0% for AFX devices and 0% for other endovascular grafts. The follow-up is limited (i.e., data is not available on all patients out to 3 years) and results from this trial may represent Type III endoleak rates under ideal circumstances, such as closer adherence to the labeling with regards to patient selection and treatment instructions.

Because the AFX endovascular graft devices with Duraply (AFX with Duraply and AFX2) have been distributed for a shorter time than the AFX with Strata endovascular graft, longer-term (i.e., out to five years and beyond) follow-up of patients receiving devices with Duraply is needed to fully define the risk of Type III endoleaks with these products. We will continue to evaluate information from several sources, including the manufacturer and real world data, about the risk of Type III endoleaks for AFX endovascular grafts with Duraply graft material (AFX with Duraply and AFX2) as compared to AFX endovascular grafts with Strata graft material, and compared to other endovascular graft systems.

As new information or recommendations become available, we will continue to share updates.

Communications About AFX Endovascular AAA System (AFX):

From the FDA :

- On October 15, 2018, the FDA issued a Class I recall (/medical-devices/medical-device-recalls/endologix-inc-recalls-afx-endovascular-aaa-systems-due-risk-type-iii-endoleaks)

to notify patients and health care providers about the risk of Type III endoleaks with use of the Endologix AFX Endovascular AAA System.

- On June 19, 2018, in an updated letter (/medical-devices/letters-health-care-providers/update-type-iii-endoleaks-associated-endovascular-graft-systems-letter-health-care-providers), the FDA informed providers that the Endologix AFX with Strata device is at greater risk for a Type III endoleak compared to other endovascular AAA graft systems.
- On September 28, 2017, the FDA issued a Letter to Health Care Providers (/medical-devices/letters-health-care-providers/type-iii-endoleaks-associated-endovascular-graft-systems-letter-health-care-providers) about the risk for Type III endoleaks with endovascular graft systems

From Endologix, Inc:

- Endologix 2016-2019 Clinical Update for AFX Endovascular AAA System (https://endologix.com/wp-content/uploads/2019/10/MM2165-Rev-01-Endologix-2016-2019-AFX-Clinical-Update.pdf) (http://www.fda.gov/about-fda/website-policies/website-disclaimer)
- Endologix Urgent: Important Safety Update - Medical Device Correction for the AFX® Endovascular AAA System (July 20, 2018) (https://endologix.com/wp-content/uploads/2018/07/AFX-Safety-Update-AFX-Users_July2018.pdf) (http://www.fda.gov/about-fda/website-policies/website-disclaimer)
- Endologix Important Safety Update: AFX™ Endovascular AAA System (December 30, 2016) (https://endologix.com/wp-content/uploads/2016/12/12-30-Physician-Letter-AFX-TIII-Endoleak-FINAL.pdf) (http://www.fda.gov/about-fda/website-policies/website-disclaimer)

Published Abstract from American College of Surgeons' Clinical Congress 2019:

- Rothenberg, Kara A. et al. Risk of Reintervention with Endologix AFX Endovascular Abdominal Aortic Aneurysm Systems in an Integrated Health Care System. Journal of the American College of Surgeons, Volume 229, Issue 4, S334.

Reporting Problems with Your Device to the FDA

If you think you had a problem with your device or a device your patient uses, we encourage you to report the problem through the MedWatch Voluntary Reporting Form (https://www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home), including, but not limited to, the following:

- Early or late device-related adverse events, such as Type III endoleaks.
- Adverse events related to secondary interventions to treat Type III endoleaks.

Health care personnel employed by facilities that are subject to the FDA's user facility reporting requirements should follow the reporting procedures established by their facilities.

Questions?

If you have questions about this communication, email the FDA's Division of Industry and Consumer Education (DICE) (/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) at DICE@FDA.HHS.GOV (mailto:DICE@FDA.HHS.GOV) or call 800-638-2041 or 301-796-7100.