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Urgent Field Safety Notice

Commercial name of the affected product: Zenith Alpha™ Thoracic Endovascular Graft

Manufacturer: William Cook Europe Aps, Sandet 6, 4632 Bjaeverskov, Denmark

Cook Reference Number: 2017FA0001

Type of action: IFU Change – Information to customers

Date: March 2017

Attention: Health Care Provider

Details on affected devices:

Zenith Alpha™ Thoracic Endovascular Graft (ZTA-)

Description of the problem:

This safety communication is to call your attention to several aspects of the new version of the Instructions for Use (IFU) for the Zenith Alpha™ Thoracic Endovascular Graft. These updates are of key importance when using the device to treat blunt thoracic aortic injury (BTAI), which is now covered under the newly approved indication for isolated lesions of the descending thoracic aorta. This Field Safety Notice is for information purposes. No devices need to be returned, and patients **already treated** for BTAI should be followed in accordance with the current IFU, since follow-up has not been amended.

Incidental findings of thrombus within the graft have been observed in approximately 25% of patients during ongoing follow-up in a clinical trial to evaluate use of the device for treatment of BTAI (none with occlusion, adverse clinical sequelae, or need for open surgical conversion/bypass due to thrombus). In the literature, the incidence of thrombus within grafts (including treatment for BTAI) ranges from 15-40%.^{1,2,3,4,5} The occurrence of graft occlusion (requiring open surgical conversion/bypass) has also been noted following endovascular treatment for BTAI.^{6,7,8} There have been five reports of graft thrombosis/occlusion during global commercial use of the device, each following treatment for BTAI. One case resulted in patient death, and three cases resulted in reintervention.

The clinical trial patients with thrombus tended to have smaller graft diameters and greater oversizing on average than the patients without thrombus. Similar trends were observed among the commercial reports as well, with those patients also tending to have a small aortic arch radius of curvature. Additionally, while approximately 50% of the clinical trial patients had an aortic diameter that tapered from large proximally to small distally (by at least 10%), a tapered graft was not consistently used (20% received a tapered graft).

Summary of Key Points from the IFU Pertinent to BTAI

The above findings underscore the importance of careful patient selection and device planning and sizing. Proximal and distal aortic diameters must be taken into account during device selection, and the use of tapered components should be considered. Furthermore, endovascular treatment requires life-long, regular follow-up to assess patient health and endovascular graft performance. This is particularly true in young patients, for whom long-term performance of endovascular grafts has not yet been established. The recommendations from the IFU below summarize key points of importance when considering use of the device for BTAI.

Summary of IFU recommendations relevant to patient selection for BTAI (Section 4):

- The Zenith Alpha Thoracic Endovascular Graft is designed to treat **aortic neck diameters no smaller than 15 mm** and no larger than 42 mm.
- Key anatomic elements that **may affect successful exclusion of the thoracic lesion include severe angulation (radius of curvature < 20 mm and localized angulation > 45 degrees)**.
- The Zenith Alpha Thoracic Endovascular Graft is not recommended for patients who cannot tolerate contrast agents necessary for intraoperative and postoperative follow-up imaging, **or who are unable to undergo, or will not be compliant with, the necessary preoperative and postoperative imaging** and implantation studies described in Section 11, IMAGING GUIDELINES AND POSTOPERATIVE FOLLOW-UP.

Summary of IFU recommendations relevant to planning and sizing for BTAI (Sections 4 and 6):

- For blunt thoracic aortic injury patients, **CTA measurements should be based on a CTA of a fully resuscitated patient.**
- Clinical experience has shown that temporary changes in aortic diameter during blood loss can lead to incorrect aortic measurement on preoperative CTA, inadequate sizing, and increased risks of graft complications, migration and endoleak, as observed during the clinical study. **If preoperative CTA is done during hemodynamic instability, repeat CTA when the patient is stable** or use IVUS at the time of the procedure to confirm diameter measurements. **For patients with blunt thoracic aortic injuries, if there is significant periaortic hematoma in the region of the subclavian artery the hematoma should not be counted in the diameter measurement, as there is a risk of oversizing the graft.**
- **Cook recommends that the Zenith Alpha Thoracic Endovascular Graft component diameters be selected as described in Tables 1 and 2.** All lengths and diameters of the devices necessary to complete the procedure should be available to the physician, especially when preoperative case planning measurements (treatment diameters and lengths) are not certain.
- Be sure to land the proximal and distal ends of the device in an aortic neck segment with a diameter that matches the initial sizing of the device. Landing in a segment that is different from the location used to size the device may potentially result in inadequate (< 10%) or **excessive (> 25%) graft diameter oversizing** and therefore migration, endoleak, thoracic aortic lesion growth, or **increased risk of thrombosis.**

Summary of IFU recommendations relevant to surveillance after treatment for BTAI (Sections 4, 7, and 11):

- The long-term performance of endovascular grafts has not yet been established. **All patients should be advised that endovascular treatment requires life-long, regular follow-up to assess their health and the performance of their endovascular graft.** Patients with specific clinical findings (e.g., endoleaks, enlarging aneurysms or ulcers, or changes in the structure or position of the endovascular graft) should receive additional follow-up. Patients should be counseled on the importance of adhering to the follow-up schedule both during the first year and at yearly intervals thereafter. **Patients should be told that regular and consistent follow-up is a critical part of ensuring the ongoing safety and effectiveness of endovascular treatment of thoracic lesions.**
- Physicians should evaluate patients on an individual basis and prescribe their follow-up relative to the needs and circumstances of each individual patient. **The recommended imaging schedule is presented in Table 3. This schedule continues to be the minimum requirement for patient follow-up and should be maintained even in the absence of clinical symptoms** (e.g., pain, numbness, weakness). Patients with specific clinical findings (e.g., endoleaks, enlarging aneurysms or ulcers, or changes in the structure or position of the stent graft) should receive follow-up at more frequent intervals.

- Patients experiencing leaks or **reduced blood flow through the graft may be required to undergo secondary endovascular interventions or surgical procedures.**
- Physicians must advise every patient that **it is important to seek prompt medical attention if he/she experiences signs of graft occlusion**, thoracic lesion enlargement or rupture. Signs of graft occlusion include, but may not be limited to, pulse-less legs, ischemia of intestines, and cold extremities.
- **Additional surveillance and possible treatment is recommended for:** type I endoleak, type III endoleak, aneurysm or ulcer enlargement > 5 mm of maximum aneurysm diameter or ulcer depth (regardless of endoleak status), migration, inadequate seal length, **graft thrombosis or occlusion**, loss of device integrity (barb separation, stent fracture, relative component migration). Consideration for reintervention or conversion to open repair should include the attending physician's assessment of an individual patient's comorbidities, life expectancy, and the patient's personal choices. Patients should be counseled that subsequent reinterventions, including catheter based and open surgical conversion, are possible following endograft placement.
- The physician should **complete the Patient ID Card and give it to the patient so that he/she can carry it with him/her at all times.** The patient should refer to the card any time he/she visits additional health practitioners, particularly for any additional diagnostic procedures (e.g., MRI).

Transmission of this Field Safety Notice:

Please share this notice with others in your organization who either use this device or follow patients treated with the device. If you need any further information or support concerning this notice, please contact your local Cook Medical Sales Representative.

Contact reference person:

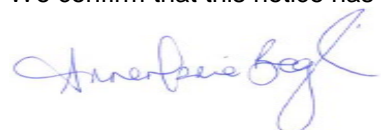
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Should you have any questions, please feel free to contact us for more information (e-mail: European.FieldAction@cookmedical.com , phone +353 61 334440).

We confirm that this notice has been notified to the appropriate Regulatory Agency.



Annemarie Beglin
Quality Systems Manager

¹ Wegener M, Gorich J, Kramer S, Fleiter T, Tomczak R, Scharrer-Pamler R et al. Thrombus formation in aortic endografts. J Endovasc Ther 2001;8(4):372-9.

² Maleux G, Koolen M, Heye S, Heremans B, Nevelsteen A. Mural thrombotic deposits in abdominal aortic endografts are common and do not require additional treatment at short-term and midterm follow-up. J Vasc Interv Radiol 2008;19(11):1558-62.

³ Wu IH, Liang PC, Huang SC, Chi NS, Lin FY, Wang SS. The significance of endograft geometry on the incidence of intraprosthetic thrombus deposits after abdominal endovascular grafting. *Eur J Vasc Endovasc Surg* 2009;38(6):741-7.

⁴ Mestres G, Maeso J, Fernandez V, Allegue N, Constenla I, Matas M. Incidence and evolution of mural thrombus in abdominal aortic endografts. *Ann Vasc Surg* 2009;23(5):627-33.

⁵ Fernandez V, Mestres G, Maeso J, Dominguez JM, Aloy MC, Matas M. Endovascular treatment of traumatic thoracic aortic injuries: short- and medium-term Follow-up. *Ann Vasc Surg* 2010;24(2):160-6.

⁶ Reich HJ, Margulies DR, Khoynezhad A. Catastrophic outcome of de novo aortic thrombus after stent grafting for blunt thoracic aortic injury. *Ann Thorac Surg* 2014;98(6):e139-e141.

⁷ Marone EM, Kahlberg A, Tshomba Y, Logaldo D, Chiesa R. Surgical conversion for intragraft thrombosis following endovascular repair of traumatic aortic injury. *J Vasc Surg* 2012;55(2):538-41.

⁸ Alvarez B, Constenla I, Maeso J, Matas M. Late thrombosis of a thoracic aorta stent graft: Therapeutic management. *J Vasc Surg* 2009;49(3):774-7.