Endologix

# 2020 ANNUAL CLINICAL UPDATE

## Ovation® Platform
Abdominal Stent Graft System

## Alto®
Abdominal Stent Graft System

# 2020 Annual Clinical Update

## Ovation® Abdominal Stent Graft System Platform (Ovation, Ovation Prime, Ovation iX)
## ALTO® Abdominal Stent Graft System

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# I. Overview

This annual clinical update provides a review of the ongoing experience with the Ovation and ALTO Abdominal Stent Graft Systems used in the treatment of abdominal aortic aneurysms. The Ovation and ALTO Systems have been commercially available in the United States since 2012 and 2020, respectively.

The Ovation PMA P120006 was approved on October 5, 2012 with subsequent approvals for Ovation Prime (P120006/S001), Ovation iX (P120006/S020), and the ALTO (P120006/S031) Abdominal Stent Graft Systems. The ALTO System represents the latest iteration of the Ovation platform. (Summary of Safety and Effectiveness, Instructions For Use).

In this update, 10 years of IDE clinical data, 5 years of Post Approval Study (PAS) data, and 8 years of worldwide commercial experience is presented.

# II. Worldwide Device Distribution

Please reference **Table 1** below for a summary of Worldwide Commercial Distribution of Ovation Implantable Devices.

**Table 1: Summary of Worldwide Commercial Distribution of Ovation**

| Device | 01 August 2019 – 31 July 2020 | Total |
|---|---|---|
| Ovation Aortic Body | 0 | 1,685 |
| Ovation Iliac Limbs/ Extensions | 0 | 5,116 |
| Ovation Prime Aortic Body | 173 | 8,715 |
| Ovation Prime Iliac Limbs/ Extensions | 484 | 19,903 |
| Ovation iX Aortic Body | 2,296 | 13,053 |
| Ovation iX Iliac Limbs | 5,440 | 31,522 |
| Ovation iX Iliac Extensions | 942 | 4,416 |
| ALTO Aortic Body | 4 | 4 |
| **TOTAL** | 9,339 | 84,414 |

# III. Clinical Evaluations

## a. Ovation Abdominal Stent Graft System Platform

**Ovation IDE Study**: Endologix successfully completed the Ovation IDE study in May 2018 which is reported in the Ovation IFU.
https://www.accessdata.fda.gov/cdrh_docs/pdf12/p120006c.pdf

**Ovation / Ovation Post Approval Study (PAS)**: A prospective, consecutively enrolling, single arm multicenter study was initiated to evaluate the long-term safety and effectiveness of the Ovation/Ovation Prime Abdominal Stent Graft System for the endovascular treatment of infrarenal abdominal aortic aneurysms in a commercial environment. The primary study endpoint was freedom from aneurysm-related mortality at five (5) years compared to a performance goal. Key secondary endpoints at 30 days, 12 months, and annually thereafter to 5 years included

- Serious Adverse Events (SAEs). All-cause mortality, AAA-related mortality, device patency, conversion to open surgical repair, endoleak, AAA enlargement, stent graft migration, device integrity, secondary endovascular procedures, and aneurysm rupture.

A total of 320 patients (161 (pivotal), 77 (continued access), and 82 (de novo) were enrolled from November 2009 to July 2015. All pivotal, continued access, and de novo patients have exited the Ovation PAS as of 01 September 2020. Reference the Ovation / Ovation Prime PAS FDA webpage: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm?t_id=489523&c_id=770

**Results of Ovation Post-Approval Study:**
Core Lab reported data from Ovation/ Ovation Prime Post-Approval Study subjects from 31 July 2015 to 30 July 2020 (5 years) is shown **Table 2** below:

**Table 2: Summary of Data from Ovation PAS subjects from 31 July 2015 to 30 July 2020**

| | | Pivotal Cohort *x/y** | Continued Access Cohort *x/y** | De novo Cohort *x/y** | Total *x/y** |
|---|---|---|---|---|---|
| **Aneurysm Related Mortality** | | 3/161 (1.9%) | 0/77 (0.0%) | 0/82 (0.0%) | 3/320 (0.9%) |
| **All- Cause Mortality** | | 35/161 (21.7%) | 17/77 (22.1%) | 15/82 (18.3%) | 67/320 (20.9%) |
| **Aneurysm Rupture** | | 1/161 (0.6%) | 1/77 (1.3%) | 0/82 (0.0%) | 2/320 (0.6%) |
| **Surgical Conversion** | | 0/161 (0.0%) | 0/77 (0.0%) | 1/82 (1.2%) | 1/320 (0.3%) |
| **All Type Endoleaks:** | **Type IA** | 0/157 (0.0%) | 0/75 (0.0%) | 2/77 (2.6%) | 2/309 (0.6%) |
| | **Type IB** | 0/157 (0.0%) | 0/75 (0.0%) | 1/77 (1.3%) | 1/309 (0.3%) |
| | **Type II** | 77/157 (49.0%) | 36/75 (48.0%) | 29/77 (37.7%) | 142/309 (46.0%) |
| | **Type IIIA** | 0/157 (0.0%) | 0/75 (0.0%) | 1/77 (1.3%) | 1/309 (0.3%) |
| | **Type IIIB** | 0/157 (0.0%) | 0/75 (0.0%) | 0/77 (0.0%) | 0/309 (0.0%) |

| | | Pivotal Cohort *x/y** | Continued Access Cohort *x/y** | De novo Cohort *x/y** | Total *x/y** |
|---|---|---|---|---|---|
| | **Type IV** | 0/157 (0.0%) | 0/75 (0.0%) | 0/77 (0.0%) | 0/309 (0.0%) |
| | **Indeterminate Origin** | 22/157 (14.0%) | 11/75 (14.7%) | 5/77 (6.5%) | 38/309 (12.3%) |
| **Aneurysm Enlargement > 5 mm** | | 22/153 (14.4%) | 7/69 (10.1%) | 12/65 (23.1%) | 41/287 (14.3%) |
| **Stent Graft Migration** | | 0/156 (0.0%) | 0/70 (0.0%) | 0/78 (0.0%) | 0/304 (0.0%) |
| **Loss of Device Patency (Occlusion)** | | 4/159 (2.5%) | 2/76 (2.6%) | 5/76 (6.6%) | 11/311 (3.5%) |
| **AAA- related Secondary Procedures** | | 33/161 (20.5%) | 20/77 (26.0%) | 7/82 (8.5%) | 60/320 (18.8%) |
| **Loss of Device Integrity**** | | 11/161 (6.80%) | 6/77 (7.80%) | 3/82 (3.70%) | 20/320 (6.30%) |

**x is the number of subjects who reported that event, and y is the number of subjects with follow-up/adequate imaging to assess the parameter.*
***The device integrity information came from Core Lab reviewed x-rays among the Pivotal and Continued Access cohorts, and was site reported for the De novo subjects.*

- One surgical conversion, due to aneurysm enlargement was reported under the post-approval study.

- With respect to secondary interventions, the subjects with stenosis or occlusion were treated with stenting, balloon angioplasty, thrombolysis, and/or thrombectomy, and four subjects were treated with a fem-fem bypass (one after an unsuccessful thrombectomy). One Continued Access subject had a resulting hematoma that required additional treatment. The other subjects have had no additional re-interventions or clinical sequelae reported after the secondary procedure.

- In total, there were 20 subjects that had Loss of Device Integrity (LDI). Among the 20 subjects, 17 had LDI due to stent fractures in the proximal stent graft. A total of 15 were single wire fractures and 2 were double wire fractures. A review of the images for the 17 subjects showed no movement of the device or collapse of the stent cage. The remaining 3 subjects had LDI due to compression/deformity of the stent. There were no associated clinical sequelae reported with these events and no device-related interventions resulted from these events. The 3 subjects with compression/deformity of the stent were described as "mild aortic graft compression", "slight compression of proximal endograft/compression distal aortic graft body", and "deformity in stent secondary to incomplete stent (expansion); proximal portion".

## b. ALTO Abdominal Stent Graft System Platform

**ALTO IDE (ELEVATE) IDE Study**: Endologix successfully completed the ALTO IDE study in March 2019 which is reported in the ALTO IFU.

https://www.accessdata.fda.gov/cdrh_docs/pdf12/P120006S031C.pdf

**ALTO Case Selection and Sizing Study (CSSS)**: A multi-center clinical evaluation was initiated to compare physician selection of patients for the ALTO device compared with Endologix Imaging Services using the same diagnostic, de-identified, CT Scan in 100 subjects. The study endpoints include a description of any differences and concordance with respect to key anatomic measurements for ALTO device sizing, general suitability for EVAR, compliance with the anatomic indications for use, and ALTO Aortic Body size selected. Fourteen (14) subjects were enrolled in the study between 30 July 2020 and 31 August 2020. Reference the ALTO CSSS PAS on FDA webpage: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm?t_id=662675&c_id=6009

For the 14 subjects enrolled, there has been 100% agreement and 0% disagreement among physician users and Endologix Imaging Services with respect to ALTO Aortic Body sizing recommendations.

**ALTO US and OUS Post-Approval Study:** The protocol for the US and OUS Post Approval RCT Study was approved by FDA on 02 October 2020. At the time of this update, there has been no enrollment in the study. Reference the ALTO RCT US and OUS PAS on FDA webpage: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm?t_id=662675&c_id=6010

# IV. Worldwide Recalls, Safety Communications and Field Safety Notices

From the time of commercial launch through 22 May 2020, there have been two safety communications regarding the Ovation iX Abdominal Stent Graft System. This section does not include information for the Ovation and Ovation Prime Abdominal Stent Graft Systems as they are no longer manufactured or marketed.

- On 06 August 2018 Endologix issued communication to physician users due to an increase in intra-operative polymer leaks identified with the Ovation iX Abdominal Stent Graft System compared to historical levels. (https://endologix.com/wp-content/uploads/2018/08/Ovation-FSN-Aug-06-Final.pdf) The polymer leaks resulted in death (AAA-related); multi-organ failure/cardiac arrest/neurological complication; local tissue necrosis; prolonged hemodynamic instability, and transient hemodynamic instability.

Investigation determined that most polymer leaks resulted from deviations to the procedural sequence related to the polymer fill and procedural steps provided in the IFU. The purpose of the safety communication was to emphasize the importance of following the polymer fill procedural sequence as instructed and provide information specifically regarding: 1) Patient Reaction; 2) Aneurysm Management; 3) Procedural Considerations; and 4) Warnings and Cautions. No changes to the IFU were required.

- On 06 May 2020, Endologix issued a communication to physician users of the Ovation iX Abdominal Stent Graft System to provide a safety update regarding polymer leaks during

implantation. (https://endologix.com/wp-content/uploads/2020/05/ENDO-Ovation-FSN-FS-0012-US-Letter-Final-5-6-20.pdf) This safety update reaffirmed treatment recommendations for patients who experience a polymer leak during implantation and provided updated information on the current rate of polymer leaks, the rate of clinical harms and the root cause. FDA identified this as a Class I recall. (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRES/res.cfm?id=181049)

The investigation determined that technical and procedural factors of the user (e.g. use of the cross over lumen before polymer fill, catheter manipulation) are not causative for the majority of polymer leaks, as was previously communicated. Adherence to the procedural steps within the Instructions for Use continues to be recommended and are not modified in this safety update. The root cause for most polymer leaks was determined to be a material weakness adjacent to the polymer fill channel which may become compromised during pressurization with liquid polymer.

The following was included as a part of Field Safety Notice as further risk mitigations for intravascular leak of polymer:

- Promptly treating the patient for potential severe hypersensitivity reaction if a polymer leak is identified
- Adhering to the procedural steps in the published device instructions for use (IFU) including existing IFU Caution and Warning statements and avoiding excessive device manipulation.

Endologix transitioned completely from Ovation iX to the ALTO Abdominal Stent Graft System at the end of October 2020. ALTO incorporates design and manufacturing changes that are intended to eliminate the areas of material weakness associated with polymer leaks. Additionally, in an effort to mitigate the procedural polymer leak risk, Endologix is committed to the ALTO Physician Training Program which incorporates best practices for polymer management. In accordance with our quality system and post-market surveillance procedures, Endologix will continue to closely monitor ALTO device performance, including any instances of polymer leak.

# V. Worldwide Commercial Experience

As part of continuous monitoring of Ovation iX lifetime device performance, the most common global product complaint category from commercialization to the current data cut (08 August 2015 – 31 July 2020) was Type IA endoleak. During this time period there were 281 Type IA events that occurred out of a total of 13,053 devices sold [281/13,053], which equals a rate of 2.15%. The root cause analysis identified that the majority of Type IA endoleaks are acute (<30 days) and the variables associated with Type IA endoleaks include the anatomical variances of reverse taper neck and juxtarenal angle. Global Medical Affairs conducted procedural training globally to all certified Ovation case supporters through a series of webinars, online modules and assessments.

The top five global product complaint categories, including Type IA endoleak as described above, are: additional endovascular procedure [91/13,053], rate= 0.70%, Type II endoleak [37/13,053], rate= 0.28%, transient hypotension [29/13,053], rate= 0.22%, and aneurysm enlargement [24/13,053], rate= 0.18%.

Endologix will continue to closely monitor Ovation device performance, including Type IA endoleak trend.

# VI. Explant Analysis

Endologix monitors product performance to ensure the ongoing quality, safety, and efficacy of its products. Upon explanation and return of a product, a historical review, engineering evaluation, and histopathological evaluations of explanted stent grafts are performed. From 01 August 2019 to 31 July 2020, Endologix did not receive any Ovation explants from commercial implant procedures.

# VII. Literature Review

The following published articles were identified that provided safety/performance data on the use of the Ovation System Platform from 01 August 2019 to 31 July 2020.

- *S Sirignano P, Capoccia L, Mansour W, Ronchey S, Accrocca F, Siani A, Mangialardi N, Speziale F.* **Type 2 Endoleak Incidence and Fate After Endovascular Aneurysms Repair in a Multicentric Series: Different Results with Different Devices?** Ann Vasc Surg. 2019 Apr; 56:224-232. doi: 10.1016/j.avsg.2018.09.009. Epub 2018 Nov 29. PubMed PMID: 30502380.

  Retrospective analysis of cohort (Ovation n=261, Excluder n=203) demonstrated there was no difference between the two groups in incidence or intervention rates for Type II endoleaks at a mean follow up time of 30 months.

- *Kontopodis N, Tavlas E, Galanakis N, Chronis C, Kafetzakis A, Tsetis D, Ioannou CV.* **Spontaneous Type Ia Endoleak Sealing in Patients Undergoing Endovascular Aneurysm Repair with the Ovation Stent Graft.** Ann Vasc Surg. 2019 Jan; 54:240-247. doi: 10.1016/j.avsg.2018.04.041. Epub 2018 Aug 6. PubMed PMID: 30092430.

  Retrospective analysis of Ovation cohort (n=8/147; 5%) with intraoperative Type Ia endoleaks showed patients were treated off-label and 75% (6/8) resolved spontaneously. Therefore 1.3% (2/147) of the patients treated off-label required intervention.

- *Swerdlow NJ, Lyden SP, Verhagen HJM, Schermerhorn ML.* **Five-year results of endovascular abdominal aortic aneurysm repair with the Ovation abdominal stent graft (ENCORE).** J Vasc Surg 2020 May;71(5):1528-1537.e2. doi: 10.1016/j.jvs.2019.06.196. Epub 2019 Sep 9.

  The analyses provided by Swerdlow et al. supports the stability of outcomes over time, includes type IA endoleaks, type I/III endoleaks, and aneurysm-related mortality. Polymer leak rate at the index procedure was 0.2%.

  The ENCORE dataset comprises 1296 subjects with various iterations of the Ovation device with follow-up through 5 years. Very low (0.7%) aneurysm-related mortality was seen through 5 years. Despite complex anatomy in half of treated patients, freedom from type IA endoleaks was 95.8% and freedom from device-related interventions was 92.4% at 5 years. The trends in clinical outcomes demonstrate the stability and durability of

endovascular aneurysm repair with the Ovation device through 5 years, without any clinically- relevant changes in safety or effectiveness. Please refer to Section IV for an overall summary of recalls, safety communications, and field safety notices for the Ovation / ALTO Platform

- *Jennifer Ash, Venita Chandra, Eva Rzucidlo, Ageliki Vouyouka, Monica Hunter.* **LUCY results show females have equivalent outcomes to males following endovascular abdominal aortic aneurysm repair despite more complex aortic morphology.** J Vasc Surg. 2020 Aug;72(2):566-575.e4. doi: 10.1016/j.jvs.2019.10.080. Epub 2020 Jan 7.

  Women undergoing EVAR with the Ovation device experienced good outcomes despite their more complex anatomy as shown in the LUCY study with 225 patients with an approximate 2:1 male to female ratio. This resulted in a much higher proportion of treated females than other EVAR studies typical of this treatment population. There was no increased risk of MAEs, readmission, all-cause death and aneurysm-related death, or endoleaks in the female cohort. No AAA ruptures or conversions were seen throughout 1-year follow-up.

# VIII. Conclusion

Based on available clinical study data and world-wide clinical experience to date, endovascular therapy with the currently marketed ALTO Abdominal Stent Graft System continues to be a viable treatment option for abdominal aortic aneurysms.

Adverse Event Reporting:

Any adverse event involving the Ovation or ALTO devices should be reported immediately to the Endologix Customer Service Department at 800-983-2284 (24 hours message service). Outside the U.S., contact your local Endologix representative. Accurate and timely reporting of adverse events by the physician users to the device manufacturer and FDA (MedWatch Form 3500) is critical for monitoring device performance and detection of potential device-related safety issues.

Patient Follow-Up and Selection:

Regular follow-up of all patients treated with the Ovation and ALTO Abdominal Stent Graft Systems is required. Physicians should tailor follow-up to the needs and circumstances of each individual patient.

**INDICATIONS FOR USE:** The Ovation® iX Abdominal Stent Graft System and the Ovation Prime® Abdominal Stent Graft System are indicated for treatment of patients with abdominal aortic aneurysms having the vascular morphology suitable for endovascular repair, including: adequate iliac/femoral access compatible with vascular access techniques (femoral cutdown or percutaneous), devices, and/or accessories; proximal aortic landing zone: with an inner wall diameter of no less than 16 mm and no greater than 30 mm at 13 mm below the inferior renal artery, and with an aortic angle of ≤ 60 degrees if proximal neck is ≥ 10 mm and ≤ 45 degrees if proximal neck is < 10 mm; distal iliac landing zone: with a length of at least 10 mm, and with an inner wall diameter of no less than 8 mm and no greater than 25 mm. (no greater than 20 mm for Ovation Prime iliac limb).

**INDICATIONS FOR USE:** The ALTO® Abdominal Stent Graft System is indicated for treatment of patients with infrarenal abdominal aortic aneurysms having the vascular morphology suitable for endovascular repair with the device, which includes the following:

- Adequate iliac/femoral access compatible with vascular access techniques (femoral cutdown or percutaneous), devices, and/or accessories,
- A proximal aortic landing zone for the sealing ring 7 mm below the inferior renal artery.
- An aortic sealing zone comprised of healthy aorta defined as:
  - Lack of significant thrombus > 8 mm in thickness; at any point along the aortic circumference at the level of 7mm below the inferior renal artery,
  - Lack of significant calcification at the level of 7 mm below the inferior renal artery,
  - Conicity < 10% as measured from the inferior renal artery to the aorta 7 mm below the inferior renal artery,
  - An inner wall diameter of no less than 16 mm and no greater than 30 mm at 7 mm below the inferior renal artery, and
  - An aortic angle of ≤ 60 degrees
- A distal iliac landing zone:
  - With a length of at least 10 mm, and
  - With an inner wall diameter of no less than 8 mm and no greater than 25 mm.

**CONTRAINDICATIONS:** The system is contraindicated for use in patients who have a condition that threatens to infect the graft and in patients with known sensitivities or allergies to the device materials including polytetrafluoroethylene [PTFE], polyethylene glycol [PEG]-based polymers, contrast agents, fluorinated ethylene propylene [FEP], titanium, nickel, platinum, or iridium.

Refer to Instructions for Use for more information concerning Indications, Contraindications, Specific Anatomic Considerations, Warnings, Precautions, and Adverse Events. Rx only.

**CAUTION:** Federal (USA) law restricts this device to sale by or on the order of a physician.

**NOTE:** Not all product components are available in every country. Please consult with your Endologix representative to confirm product availability. CE marked.



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