GORE® EXCLUDER®
Iliac Branch Endoprosthesis

ANNUAL CLINICAL UPDATE

July 1, 2020 through
June 30, 2021

Together, improving life

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Overview

This Annual Clinical Update (ACU) provides a review of the ongoing experience with the GORE® EXCLUDER® Iliac Branch Endoprosthesis (IBE) used in the treatment of common iliac artery aneurysms (CIAA) and aorto-iliac aneurysms (AIA). In this update, five years of pivotal study data and the most recent year of worldwide commercial experience are presented.

The IBE is an implantable endoprosthesis which consists of two modular components and associated delivery systems. The two components are the Iliac Branch Component (IBC) and the Internal Iliac Component (IIC). The graft material of both is comprised of expanded polytetrafluoroethylene (ePTFE) and fluorinated ethylene propylene (FEP) and is attached to and supported by nitinol wire along its external surface. An ePTFE/FEP sleeve is attached to the endoprosthesis and is used to constrain the endoprosthesis on the leading end of the delivery catheter for implantation. Radiopaque markers are attached to both the stent graft and delivery catheter to facilitate fluoroscopic visualization and orientation. Deployment of each component is achieved by pulling a deployment line that releases the sleeve and allows the stent graft to self-expand in vivo.

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INSTRUCTIONS FOR USE

The most up-to-date version of the *Instructions for Use* (IFU) can be found at the web address https://eifu.goremedical.com and searching for the device part number or prefix (e.g., "CEB"). Additional details on the GORE® EXCLUDER® Iliac Branch Endoprosthesis can be found in the Summary of Safety and Effectiveness Data (SSED) document on the United States FDA website at the web address: https://www.accessdata.fda.gov/cdrh_docs/pdf2/P020004S123B.pdf.

Table 1 provides a brief regulatory approval history of the device.

Table 1: GORE® EXCLUDER® Iliac Branch Endoprosthesis regulatory approval history

Country/Region	Approval date
Europe	October 2013
USA	February 2016
Canada	February 2016
Australia/New Zealand	January 2015
Japan	November 2017
Brazil	August 2019
China	December 2021

Worldwide device distribution

From the European Union approval date of October 2, 2013 through June 30, 2021, more than 25,000 IBEs have been distributed worldwide.

This ACU includes commercial distribution between July 1, 2020 – June 30, 2021, during which time approximately 5,000 IBEs were distributed worldwide, consisting of a total of approximately 10,000 components.

Clinical evaluations

The evaluation of the IBE for the Treatment of Common Iliac Artery Aneurysms or Aorto-iliac Aneurysms Clinical Study, the IBE 12-04 Study (IDE G130038; NCT 01883999) is a prospective, nonrandomized, multicenter, single-arm evaluation study to assess the safety and effectiveness of the IBE for treatment of patients with common iliac artery aneurysms (CIAA) or aortoiliac aneurysms (AIA).

The IBE 12-04 Study was a multicenter study with a maximum of up to 50 sites and up to 200 patients treated with the IBE (minimum of 60 patients in the IBE 12-04 primary enrollment and up to 140 continued access patients). Enrollment began in October 2013 and closed in April 2016. Five-year follow-up was completed in April 2021. Further details of the IBE 12-04 Study is provided here: Details of clinical pivotal study IBE 12-04

65 patients were enrolled at 28 investigational sites in primary enrollment. An additional 35 subjects were enrolled at 20 sites in a continued access cohort. A total of 94 patients underwent unilateral IBE placement and four patients underwent bilateral IBE placement. Two patients withdrew prior to the IBE procedure.

The primary safety endpoint was a composite of the following events through 30 days post-treatment:

- Death
- Stroke
- Myocardial infarction
- Bowel ischemia
- Paraplegia
- Respiratory failure
- Renal failure
- Conversion to open surgical repair

The primary effectiveness endpoint was a composite of the following events through the six-month follow-up visit:

- Reintervention on the iliac branch component or the internal iliac component due to Type Ib or Type III endoleak as determined by the Clinical Events Committee (CEC).
- Complete loss of blood flow in the leg of the Iliac Branch Component or the Internal Iliac Component due to thrombus or device failure as assessed by an independent core laboratory.
- Reintervention on the Iliac Branch Component or the Internal Iliac Component to re-establish patency due to 60% occlusion or greater as determined by the CEC.

Final follow-up data from the IBE 12-04 Study subjects are presented below in **Table 2**. Five-year follow-up has been completed for all subjects as of the data export on July 19, 2021.

Twelve subjects (12.2%) have received reinterventions. Six subjects have received embolization for Type II endoleak, three received additional stents, two received thrombectomy and one subject had conversion to open repair due to an infection.

Table 2: IBE 12-04 Study through five years of follow-up[*,†]

	1 month	6 months	12 months	24 months	36 months	48 months	60 months	Total
Subjects eligible for follow-up	98	98	93	89	80	74	68	98
Subjects discontinued or lost to follow-up	0	5	4	9	6	6	15	45
Aneurysm-related mortality	0/98	0/98	0/91	0/86	0/77	0/70	0/66	0/98
Aneurysm rupture	0/91	0/85	0/78	0/69	0/58	0/52	0/45	0/96
Conversions	0/98	0/98	0/91	0/86	1/77 (1.3%)	0/70	0/66	1/98 (1.0%)
Type I endoleak	0/89	0/81	0/78	0/70	0/58	1/52 (1.9%)	1/45 (2.2%)	1/95 (1.1%)
Type Ia endoleak	0/89	0/81	0/78	0/70	0/58	1/52 (1.9%)	1/45 (2.2%)	1/95 (1.1%)
Type Ib endoleak	0/89	0/81	0/78	0/70	0/58	0/52	0/45	0/95
Type III endoleak	0/89	0/81	0/78	0/70	0/58	0/52	0/45	0/95
Diameter enlargement ≥ 5 mm (Core Lab orthogonal view)		0/70	0/67	0/51	0/42	0/1	-	0/78
Common iliac artery[‡]	-	0/81	0/78	1/68 (1.5%)	0/56	0/49	0/45	1/84 (1.2%)
Abdominal aorta	-	0/84	2/80 (2.5%)	4/70 (5.7%)	5/59 (8.5%)	11/52 (21.2%)	11/46 (23.9%)	15/87 (17.2%)
Prosthesis migration	0/92	0/88	0/83	0/72	0/60	0/53 (1.9%)	1/47 (2.1%)	1/96 (1.0%)
Occlusions								
Iliac branch component	1/91 (1.1%)	0/85	0/78	0/69	0/58	0/52	0/45	1/96 (1.0%)
Internal iliac component	5/91 (5.5%)	4/85 (4.7%)	3/78 (3.8%)	2/69 (2.9%)	0/58	0/52	0/45	5/96 (5.2%)
Fracture	0/44	1/43 (2.3%)	0/34	0/32	0/27	1/24 (4.2%)	1/24 (4.2%)	1/60 (1.7%)

* Denominators used in calculation of percentages are number of subjects at risk (for aneurysm related mortality and conversion) or with an evaluable result (for all other outcomes which are derived from Core Lab assessment of imaging in effectiveness eligible subjects).

† Study period definitions: 1 month (15-59 days); 6 months (60-242 days); 12 months (243-546 days); 24 months (547-911 days); 36 months (912-1,275 days); 48 months (1,276-1,640 days); 60 months (1,641-2,006 days); Total (15-2,006 days).

‡ Denominators for subjects with unilateral IBE placement, assessing diameter change of common iliac artery on the IBE side.

Bilateral IBE placement

In order to supplement the information about bilateral IBE placement, IBE 12-04 bilateral device placement study results (n = 4) are presented alongside results from the subsets of bilateral placement patients enrolled in GREAT (GRT 10-11) (n = 15) and IceBERG (n = 28) as shown in **Tables 3 and 4**.

GREAT (GRT 10-11) is a global observational registry designed to obtain data on device performance and clinical outcomes of patients with aortic disease pathologies treated with all commercially available Gore endovascular aortic products. GREAT is a prospective, observational registry that is a non-randomized, multicenter, single-arm evaluation. The registry includes patients with various aortic disease pathologies and treated with any commercially available Gore endovascular aortic product.

This study is being conducted under an IDE within the U.S. (IDE G120012/S004; NCT 01658787).

IceBERG is a European observational registry to collect data on the preservation of the internal iliac artery (hypogastric artery) after treatment for common iliac artery/abdominal aortic aneurysm disease using the GORE® EXCLUDER® AAA Endoprosthesis and IBE (NCT02345005). This study is in two parts:

- A retrospective registry of patients implanted with the IBE from 13 sites in the Netherlands after CE mark was obtained, to get an initial insight on the feasibility and safety of this procedure.
- A prospective registry of patients implanted with the IBE from 11 sites in Europe and one site in New Zealand, in order to gain more robust data on the efficacy of the device in maintaining hypogastric artery patency.

Table 3: Summary of technical success, bilateral IBE placement in IBE 12-04 Study, GREAT and IceBERG

	IBE 12-04 bilateral IBE	GREAT bilateral IBE	IceBERG bilateral IBE
Number of patients	4	15	28
Number of patients with information available	4	12	28
Successful access	4 (100.0%)	11 (91.7%)	28 (100.0%)
Successful deployment of the IBE (and GORE® EXCLUDER® AAA Device) in the intended location	4 (100.0%)	11 (91.7%)	28 (100.0%)
Successful removal of all IBE delivery catheters	4 (100.0%)	12 (100.0%)	28 (100.0%)
Patent IBE (and GORE® EXCLUDER® AAA Device) on completion angiography	4 (100.0%)	11 (91.7%)	28 (100.0%)
Absence of Type I and Type III endoleak on completion angiography	4 (100.0%)	10 (83.3%)	27 (96.4%)
Successful access site closure	4 (100.0%)	12 (100.0%)	28 (100.0%)

Table 4: Summary of key outcomes, bilateral IBE placement in IBE 12-04 Study (core lab), GREAT and IceBERG*

	IBE 12-04 bilateral IBE	GREAT bilateral IBE	IceBERG bilateral IBE
Number of patients	4	15	28
Number of patients with information available	4	12	27
Follow-up time (median)	1,516 days	1,769 days	24 months
Death	1 (25.0%)	4 (33.3%)	0
Aneurysm-related death	0	1 (8.3%)	0
Aneurysm rupture	0	1 (8.3%)	1 (3.7%)
Secondary procedure	0	3 (25.0%)	2 (7.4%)
Embolization	0	0	0
Thrombectomy	0	0	1 (3.7%)
Other	0	3 (25.0%)	1 (3.7%)
Conversion to surgical repair	0	1 (8.3%)	0
Endoleak	3 (75.0%)	5 (41.7%)	14 (51.9%)
Type I	0	1 (8.3%)	1 (3.7%)
Type II	3 (75.0%)	4 (33.3%)	11 (40.7%)
Type III	0	0	0
Indeterminate	0	0	2 (7.4%)
Aneurysm enlargement	0	4 (33.3%)	2 (7.4%)
Prosthesis migration	0	0	0
Loss of patency in device	0	0	0
Loss of device integrity	0	0	0

* Denominators are number of patients with key outcome information provided by the study sites, regardless of the follow-up status.

Worldwide recalls, safety communications and field safety notices

During the period covered by this annual clinical update, July 1, 2020 – June 30, 2021, there have been no recalls, safety communications or field safety notices associated with the IBE.

Worldwide commercial experience

The data presented in **Table 4** summarize adverse events from worldwide commercial experience that occurred in the past year from July 1, 2020 to June 30, 2021. During this time period, more than 5,000 IBE have been distributed. Adverse event reports presented in **Table 5** are similar or lower than those reported in prior annual clinical updates. Each reported adverse event is not mutually exclusive and may contain multiple adverse events. Since IBE is used in conjunction with the GORE® EXCLUDER® AAA Device, adverse events unique to IBE and not related to the GORE® EXCLUDER® AAA Device are called out in parenthesis.

The worldwide commercial experience with the IBE has remained consistent with the acceptable performance exhibited in previous years.

Table 5: Summary of IBE worldwide performance (July 1, 2020 – June 30, 2021)

Adverse event	Number of events
Aneurysm-related death*	1 (0 unique)
Post-procedure aneurysm rupture	3 (0 unique)
Aneurysm enlargement†	4 (1 unique)
Conversion	3 (0 unique)
Migration‡	0
Device occlusion	5 (2 unique)
Infection	2 (0 unique)
Infolding	1
Type III endoleak§	13 (3 unique)
Deployment related events	5 (5 unique)
Stent fracture	0

* Aneurysm-related deaths are defined as any deaths within 30 days or due to aneurysm rupture, a primary or secondary procedure or surgical conversion.[1]

† Aneurysm enlargement in this table is defined as any reported enlarging aneurysm with and without endoleak ≥ 5 mm or if no measurement is reported.

‡ During commercial use, migration is defined as any report of post-procedure device movement.

§ Ten of the Type III endoleaks reported occurred at the junction of the proximal portion of the IBE and bridging contralateral leg component. The remaining three occurred with off-label use of non-indicated small diameter stent grafts in place of the Internal Iliac Branch Component.

Explant analysis

The data presented in **Table 6** summarize the number of IBE explants and the corresponding reason for explant from July 1, 2020 to June 30, 2021. Of the three reported surgical conversions performed, none of the explanted devices were returned for analysis. There were no device integrity observations reported with any of the explanted devices.

Table 6: Primary cause of explant (July 1, 2020 – June 30, 2021)

Reason for explant	Number of occurrences
Implantation difficulties	0
Rupture	0
Aneurysm enlargement without endoleak	0
Aneurysm enlargement with endoleak	1
Endoleak	0
Migration	0
Infection	2
Aortoenteric fistula	0
Occlusion	0
Incidental autopsy	0
Other	0
Total cases	**3**

Literature review

The following peer-reviewed literature articles published between July 1, 2020 and June 30, 2021 describe the safety and effectiveness of the IBE.

DeRoo, et al. describes the results of a post hoc analysis of the prospective, multicenter IBE 12-04 pivotal trial. The objective of the study was to identify risk factors associated with adverse iliac events (AIE) following IBE implantation. Of 98 patients with 101 treated iliac arteries, there were a total of eight AIEs. In summary, patients with small diameter (< 10 mm) and more tortuous internal iliac arteries were at greater risk of AIE's than those without. Specifically, lack of endograft conformation within the internal iliac landing zone was a significant indicator or AIE risk (36% vs. 4%, $P = .004$).[1]

Fernandez, et al. reports on the results of the IBE device in the retrospective, multicenter GALIBER registry. The report includes data from 81 patients with 105 treated iliac arteries from five hospitals from January 2014 to May 2019. Of 33 patients with bilateral iliac aneurysms, 24 had bilateral IBE placed and nine had embolization of the contralateral hypogastric artery. Technical success was achieved in all but one IBE implantation (104/105 successful) and there were no IBE-related endoleaks observed in follow-up. IBE patency was 98.1% during follow-up (55-1,789 days). In patients with contralateral hypogastric embolization, 30% experienced ischemic complications.[2]

Conclusion

Based on available clinical study data and worldwide clinical experience to date, endovascular therapy with the IBE continues to be a viable treatment option for the treatment of aneurysmal disease associated with the iliac arteries.

Patient follow-up and selection

Regular follow-up of all patients treated with this device is required. Worldwide commercial experience and clinical data demonstrate that some adverse events may become apparent over time. As stated in the IFU, regular and consistent follow-up is a critical part of ensuring continuing safety and efficacy of aortic endovascular repair. Patients with specific clinical findings such as endoleak and/or aneurysm enlargement should receive enhanced follow-up. Physicians should tailor patient follow-up to the needs and circumstances of each individual patient. As outlined in the IFU, critical factors for successful clinical outcomes include:

- Appropriate patient selection, including:
  - Adequate iliac/femoral access.
  - Minimum common iliac diameter of 17 mm at the proximal implantation zone of the IBE.
  - External iliac artery treatment range of 6.5 – 25 mm and seal zone length of at least 10 mm.
  - Internal iliac artery treatment range of 6.5 – 13.5 mm and seal zone length of at least 10 mm.
  - Adequate length from the lowest major renal artery to the internal iliac artery to accommodate the total endoprosthesis length, calculated by adding the minimum lengths of required components, taking into account appropriate overlaps between components.
- Device selection in accordance with the IFU.
- Device deployment in accordance with the IFU.
- Appropriate and timely patient follow-up.

ADVERSE EVENT REPORTING

The accurate and timely reporting of adverse events by users is critical for monitoring device performance and detection of device-related safety issues. Any adverse event involving the IBE should be reported to Gore immediately. To report an event in the U.S., call 800 437 8181.

References

1. DeRoo E, Harris D, Olson S, *et al*. Conformability of the GORE® EXCLUDER® Iliac branch endoprosthesis is associated with freedom from adverse iliac events. *Journal of Vascular Surgery* 2021; 74(5):1558-1564.
2. Méndez Fernández, A., Fernández Noya, J., Mosquera Arochena, N.J., *et al*. Results of the Galician registry in the treatment of complex aortoiliac aneurysms with the GORE® EXCLUDER® Iliac Branch Endoprosthesis (GALIBER). *Vascular*. June 2021.

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INDICATIONS FOR USE IN THE U.S.: Iliac Branch and Internal Iliac Components The GORE®EXCLUDER® Iliac Branch Endoprosthesis (IBE) is intended to be used with the GORE® EXCLUDER® AAA Endoprosthesis or the GORE® EXCLUDER® Conformable Endoprosthesis to isolatethe common iliac artery from systemic blood flow and preserve blood flow in the external iliac and internal iliac arteries in patients with acommon iliac or aortoiliac aneurysm, who have appropriate anatomy, including: Adequate iliac/femoral access; minimum common iliacdiameter of 17 mm at the proximal implantation zone of the IBE; external Iliac artery treatment diameter range of 6.5–25 mm and seal zonelength of at least 10 mm; internal iliac artery treatment diameter range of 6.5–13.5 mm and seal zone length of at least 10 mm; adequatelength from the lowest major renal artery to the internal iliac artery to accommodate the total endoprosthesis length, calculated by adding theminimum lengths of required components, taking into account appropriate overlaps between components. **GORE® EXCLUDER® Components used in conjunction with GORE® EXCLUDER® Iliac Branch Endoprosthesis: Trunk-Ipsilateral Leg Component.** The Trunk-IpsilateralLeg is intended to provide proximal seal and fixation for the endovascular repair of the aneurysm. For more information on the Trunk-IpsilateralLeg Component indications for use and deployment, see the GORE® EXCLUDER® AAA Endoprosthesis or the GORE® EXCLUDER® ConformableEndoprosthesis *Instructions for Use*. **Contralateral Leg Endoprosthesis Component.** The Contralateral Leg Endoprosthesis is intended tobridge the GORE® EXCLUDER® Device Trunk-Ipsilateral Component to the GORE® EXCLUDER® Iliac Branch Endoprosthesis following deploymentof the GORE® EXCLUDER® Iliac Branch Endoprosthesis. Additionally, the Contralateral Leg Endprosthesis is intended to be used for distal extension of the Iliac Branch Component in the external iliac artery. The Iliac Branch Component can treat external iliac artery diameters up to 13.5 mm. This ability to extend the Iliac Branch Component distally with any Contralateral Leg Endoprosthesis expands the external iliac artery treatment range up to 25 mm. For more information on the Trunk-Ipsilateral Leg and Contralateral Leg Endoprosthesis Component indications for use and deployment, see the GORE® EXCLUDER® AAA Endoprosthesis *Instructions for Use*. **Aortic Extender and Iliac Extender Components.** The Aortic and Iliac Extender Components can be used after deployment of the GORE® EXCLUDER® Iliac Branch and GORE® EXCLUDER® AAA Endoprostheses or the GORE®EXCLUDER® Conformable Endoprosthesis. These extensions are used when additional length and/or sealing for aneurysmal exclusion is desired. For more information on Aortic Extender and Iliac Extender indications for use and deployment, see the GORE®EXCLUDER® AAA Endoprosthesis or the GORE® EXCLUDER® Conformable Endoprosthesis *Instructions for Use*. **CONTRAINDICATIONS:** The GORE® EXCLUDER® Iliac Branch Endoprosthesis is contraindicated in: Patients with known sensitivities or allergies to the device materials. All components of the GORE® EXCLUDER® Iliac Branch Endoprosthesis, the GORE® EXCLUDER® AAA Endoprosthesis and the GORE® EXCLUDER® Conformable Endoprosthesis contain ePTFE, FEP, nitinol (nickel-titanium alloy) and gold. Patients with a systemic infection who may be at increased risk of endovascular graft infection. Refer to *Instructions for Use* at eifu.goremedical.com for a complete description of all applicable indications, warnings, precautions and contraindicationsfor the markets where this product is available. ℞ Only

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