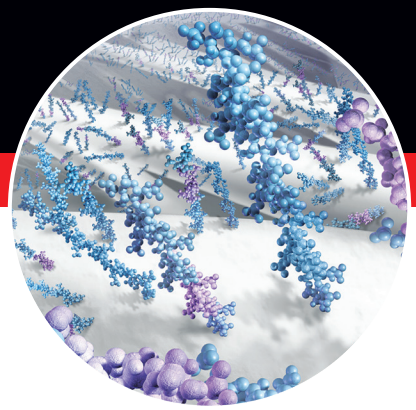
Heparin Induced Thrombocytopenia Type II (HIT) and the CBAS Heparin Surface



There is no evidence to support a causative or contributory association of the CBAS Heparin Surface and the condition of HIT*

The risk of HIT for patients receiving systemic heparin is low.

- The incidence of HIT in patients receiving systemic heparin is low, < 1–5%, depending upon the patient population and the type of heparin used[1]
- The incidence of HIT in the pediatric patient population is extremely low. According to the Kids' Inpatient Database (KID),[2] in all patients less than 1 year of age (n = 4,252,702), there were only 20 HIT diagnoses. Additionally, only 3 out of 1,852 patients who were implanted with any type of pediatric shunt were diagnosed with HIT (0.16%).
- Analysis of reports received by Gore related to vascular devices with the CBAS Heparin Surface yield an incidence of suspected HIT events of less than 0.006%. In some patients with suspected HIT, devices with the CBAS Heparin Surface have remained implanted without HIT-related clinical sequelae.[3]

In patients enrolled in various studies of Gore products having the CBAS Heparin Surface that tracked adverse events, there have been no reports of contribution of the CBAS Heparin Surface to HIT or the formation or persistence of HIT antibodies.[4-14]

- In a study by Heyligers *et al*,[15] HIT-inducing antibodies were not detected in any of the patients (n = 10) that received a GORE® PROPATEN® Vascular Graft, even six weeks post-implantation
- In a study by Chadda *et al*,[16] a series of 45 patients who received a GORE® VIABAHN® Endoprosthesis with Heparin Bioactive Surface† were monitored for HIT (defined as a platelet count fall of greater than 50%). None of the patients experienced HIT.‡
- In HIT studies conducted on patients who received non-Gore devices with the CARMEDA® BioActive Surface§ (n = 30 and n = 57), the presence of the CARMEDA® BioActive Surface was not found to contribute to an increased rate of HIT antibody formation or persistence of the antibodies over time[17,18]

Administration of systemic heparin confounds interpretation of the cause of HIT events.[3]

- As with most interventions in the vascular system, the administration of systemic heparin in these procedures makes it impossible to conclude whether or not the device with the CBAS Heparin Surface contributed to the development of HIT
- The total amount of heparin on a device with the CBAS Heparin Surface is extremely small in comparison to a therapeutic dose of heparin (data on file 2017, 2018; W. L. Gore & Associates, Inc.; Flagstaff, AZ.)
- There are four published single-patient case reports describing HIT in patients having a Gore device with the CBAS Heparin Surface.[19-22] Each patient was given several thousand IU of unfractionated heparin systemically during the surgical implantation of the device.

Based on the lack of empirical evidence for a causal link between the CBAS Heparin Surface and HIT, it can be reasonably concluded that the risk of HIT involving Gore devices having the CBAS Heparin Surface is very low.

- Nonetheless, the IFUs for Gore devices with the CBAS Heparin Surface acknowledge the potential for HIT in association with any vascular procedure and Gore devices with the CBAS Heparin Surface are contraindicated for use in patients with known hypersensitivity to heparin, including those patients who have had a previous incident of HIT Type II

* Clinical experience of published literature, product surveillance reviews and analysis of clinical data for devices with the CBAS Heparin Surface.
† As used by Gore, Heparin Bioactive Surface refers to Gore's proprietary CBAS Heparin Surface.
‡ Also referred to as the GORE® VIABAHN® Endoprosthesis with PROPATEN Bioactive Surface in some regions.
§ The heparin technology of the CARMEDA® BioActive Surface is marketed as the CBAS Heparin Surface for Gore vascular devices.

References

1. Linkins LA, Lee DH. Frequency of heparin-induced thrombocytopenia. In: Warkentin TE, Greinacher A, eds. *Heparin-Induced Thrombocytopenia*. 5th ed. New York, NY: Informa Healthcare USA; 2012;(4):110-150.
2. Kids' Inpatient Database (KID). Healthcare Cost and Utilization Project (HCUP). Rockville, MD: Agency for Healthcare Research and Quality; 2019. https://www.hcup-us.ahrq.gov/db/nation/kid/kiddbdocumentation.jsp . Updated September 18, 2019. Accessed November 8, 2019.
3. Kasirajan K. Outcomes after heparin-induced thrombocytopenia in patients with Propaten vascular grafts. *Annals of Vascular Surgery* 2012;26(6):802-808.
4. Lindholt JS, Gottschalksen B, Johannesen N, *et al*. The Scandinavian Propaten® Trial – 1-year patency of PTFE vascular prostheses with heparin-bonded luminal surfaces compared to ordinary pure PTFE vascular prostheses – a randomised clinical controlled multi-centre trial. *European Journal of Vascular & Endovascular Surgery* 2011;41(5):668-673. [n = 546]
5. U.S. Food and Drug Administration. Center for Devices and Radiological Health. 510(k) Premarket Notification. GORE PROPATEN Vascular Graft, Summary of Substantial Equivalence. K062161. https://www.accessdata.fda.gov/cdrh_docs/pdf6/K062161.pdf . November 9, 2006. Accessed November 8, 2019.
6. Hugl B, Nevelsteen A, Daenens K, *et al.*; PEPE II Study Group. PEPE II - a multicenter study with an end-point heparin-bonded expanded polytetrafluoroethylene vascular graft for above and below knee bypass surgery: determinants of patency. *Journal of Cardiovascular Surgery* 2009;50(2):195-203. [n = 139]
7. Samson RH, Morales R, Showalter DP, Lepore MR Jr., Nair DG. Heparin-bonded expanded polytetrafluoroethylene femoropopliteal bypass grafts outperform expanded polytetrafluoroethylene grafts without heparin in a long-term comparison. *Journal of Vascular Surgery* 2016;64(3):638-647. https://www.sciencedirect.com/science/article/pii/S0741521416008272
8. Bismuth J, Gray BH, Holden A, Metzger C, Panneton J; VBX FLEX Study Investigators. Pivotal study of a next-generation balloon-expandable stent-graft for treatment of iliac occlusive disease. *Journal of Endovascular Therapy* 2017;24(5):629-637. http://journals.sagepub.com/doi/full/10.1177/1526602817720463
9. Glickman MH, Burgess J, Cull D, Roy-Chaudhury P, Schanzer H. Prospective multicenter study with a 1-year analysis of a new vascular graft used for early cannulation in patients undergoing hemodialysis. *Journal of Vascular Surgery* 2015;62(2):434-441. http://www.sciencedirect.com/science/article/pii/S0741521415003651
10. Saxon RR, Chervu A, Jones PA, *et al*. Heparin-bonded, expanded polytetrafluoroethylene-lined stent graft in the treatment of femoropopliteal artery disease: 1-year results of the VIPER (Viabahn Endoprosthesis with Heparin Bioactive Surface in the Treatment of Superficial Femoral Artery Obstructive Disease) trial. *Journal of Vascular & Interventional Radiology* 2013;24(2):165-173.
11. Bosiers M, Deloose K, Callaert J, *et al*. Superiority of stent-grafts for in-stent restenosis in the superficial femoral artery: twelve-month results from a multicenter randomized trial. *Journal of Endovascular Therapy* 2015;22(1):1-10.
12. Zeller T, Peeters P, Bosiers M, *et al*. Heparin-bonded stent-graft for the treatment of TASC II C and D femoropopliteal lesions: the Viabahn-25 cm Trial. *Journal of Endovascular Therapy* 2014;21(6):765-774.
13. Vesely T, DaVanzo W, Behrend T, Dwyer A, Aruny J. Balloon angioplasty versus Viabahn stent graft for treatment of failing or thrombosed prosthetic hemodialysis grafts. *Journal of Vascular Surgery* 2016;64(5):1400-1410.e1. http://www.sciencedirect.com/science/article/pii/S0741521416301756
14. Ohki T, Kichikawa K, Yokoi H, *et al*. Outcomes of the Japanese multicenter Viabahn trial of endovascular stent grafting for superficial femoral artery lesions. *Journal of Vascular Surgery* 2017;66(1):130-142.e1. http://www.sciencedirect.com/science/article/pii/S074152141730383X
15. Heyligers JMM, Lisman T, Verhagen HJM, Weeterings C, de Groot PG, Moll FL. A heparin-bonded vascular graft generates no systemic effect on markers of hemostasis activation or detectable heparin-induced thrombocytopenia– associated antibodies in humans. *Journal of Vascular Surgery* 2008;47(2):324-329. [n = 10]
16. Chadda N, Museitif R, Djelmami-Hani M, *et al*. Heparin-bonded VIABAHN Stent Graft for SFA lesions: incidence of stent thrombosis and heparin-induced thrombocytopenia. Abstract presented at the Transcatheter Cardiovascular Therapeutics (TCT) 20th Annual Scientific Symposium; October 12 -17, 2008; Washington, DC. *American Journal of Cardiology* 2008;102(8)Supplement 1:221i. TCT-586.
17. Koster A, Loebe M, Sodian R, *et al*. Heparin antibodies and thromboembolism in heparin-coated and noncoated ventricular assist devices. *Journal of Thoracic & Cardiovascular Surgery* 2001;121(2):331-335.
18. Koster A, Sanger S, Hansen R, *et al*. Prevalence and persistence of heparin/platelet factor 4 antibodies in patients with heparin coated and noncoated ventricular assist devices. *Asaio Journal* 2000;46(3):319-322.
19. Wheatcroft MD, Greco E, Tse L, Roche-Nagle G. Heparin-induced thrombocytopenia in the presence of a heparin-bonded bypass graft. *Vascular* 2011;19(6):338-341.
20. Gabrielli R, Siani A, Rosati MS, *et al*. Heparin-induced thrombocytopenia type II because of heparin-coated polytetrafluoroethylene graft used to bypass. *Annals of Vascular Surgery* 2011;25(6):840.e9-840.e12.
21. Thakur S, Pigott JP, Comerota AJ. Heparin-induced thrombocytopenia after implantation of a heparin-bonded polytetrafluoroethylene lower extremity bypass graft: a case report and plan for management . *Journal of Vascular Surgery* 2009;49(4):1037-1040.
22. Blas JVV, Carsten CG III, Gray BH. Heparin-induced thrombocytopenia associated with a heparin-bonded stent graft. *Annals of Vascular Surgery* 2016;33:227.e1-227.e4.

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INDICATIONS FOR USE: GORE® PROPATEN® Vascular Grafts are intended for use as vascular prostheses for replacement or bypass of diseased vessels in patients suffering occlusive or aneurysmal diseases, in trauma patients requiring vascular replacement, for dialysis access or for other vascular procedures. **CONTRAINDICATIONS:** A. DO NOT use the GORE® PROPATEN® Vascular Graft in patients with known hypersensitivity to heparin, including those patients who have had a previous incidence of Heparin-Induced Thrombocytopenia (HIT) type II. B. DO NOT use any configuration of GORE® PROPATEN® Vascular Grafts with Removable Rings, Non-Removable Rings or Integrated Rings for coronary artery bypass or cerebral reconstruction procedures. C. DO NOT use GORE® PROPATEN® Vascular Grafts as a patch. If cut and used as a patch, GORE® PROPATEN® Vascular Grafts may lack adequate transverse strength. Refer to *Instructions for Use* at eifu.goremedical.com for a complete description of all applicable indications, warnings, precautions and contraindications for the markets where this product is available. ℞ Only

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eifu.goremedical.com

W. L. Gore & Associates, Inc.
Flagstaff, AZ 86004

+65 67332882 (Asia Pacific)
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