

	Safety and Effectiveness Evaluation of Eximo's B-Laser™ Atherectomy Device, in Subjects Affected with PAD – a Clinical Study Protocol Synopsis	Date: 20 Nov 2016
PRODUCT: Eximo Medical B-Laser™ for PAD		Page 1 of 3
Document number: EX-PAD-01		Revision: 05

Study Title:	Safety & effectiveness evaluation of Eximo's B-Laser™ Atherectomy Device, in subjects affected with Peripheral Arterial Disease (PAD), Study Protocol ID: EX-PAD-01 [NCT02556255]
Study Design:	Prospective, single-arm, multi-center, international, open-label, non-randomized clinical study.
Objective:	To assess the safety and efficacy of the use of Eximo's B-Laser™ catheter in subjects affected with PAD in lower extremity arteries.
Subject Population:	Men and Women with symptomatic occlusive PAD in lower extremity arteries that are scheduled for PAD endovascular intervention and are eligible according to protocol inclusion / exclusion criteria.
Study Endpoints:	<p><u>Primary Endpoint - Safety:</u></p> <p><u>30 day Freedom from the following Major Adverse Events (MAE):</u></p> <ul style="list-style-type: none"> ○ Need for emergency surgical revascularization of the target limb ○ Unplanned target limb amputation above the ankle ○ Clinically driven target lesion revascularization (TLR) ○ Cardiovascular related deaths <p><u>Perioperative (until discharge) freedom from the following Device/Procedure¹ Related Adverse Events (AE):</u></p> <ul style="list-style-type: none"> ○ Clinically Significant target vessel's Perforations requiring intervention ○ Clinically Significant target vessel's Dissections requiring intervention ○ Clinically Significant target vessel's distal embolization or in-situ thrombus requiring intervention ○ Clinically significant target vessel's Pseudo-aneurysm requiring intervention <p><u>Primary Endpoint – Effectiveness - Technical Success:</u></p> <ul style="list-style-type: none"> ○ Ability of the B-Laser™ to cross the target lesion stenosis over the wire while the stenotic flow diameter is smaller than the B-Laser™ diameter. <p><u>Secondary Endpoint - Safety:</u></p> <p><u>Perioperative (until discharge) freedom from the following Device/Procedure¹ Related Adverse Events:</u></p> <ul style="list-style-type: none"> ○ Emboli, defined as a new occlusion of any visualized runoff vessel which cannot be reversed with an intravascular vasodilator ○ Flow limitation dissection <p><u>30 day freedom from the following Device/Procedure¹ Related Adverse Events:</u></p> <ul style="list-style-type: none"> ○ Clinically Significant target vessel's Dissections requiring intervention ○ Clinically Significant target vessel distal embolization or in-situ thrombus requiring intervention ○ Clinically Significant target vessel's Pseudo-aneurysm requiring intervention <p><u>Secondary Endpoints – Effectiveness:</u></p> <ul style="list-style-type: none"> ○ The ability of the B-Laser™ device to achieve a post-intervention residual diameter stenosis of <30% with adjunctive therapy as assessed by fluoroscopic angiography in cases where adjunctive therapy is medically applicable ○ Improved Ankle-Brachial Index (ABI) at 30 days, 6 months and 12 months post B-Laser™ device procedure compared to baseline. ○ Improved Rutherford Classification at 30 days, 6 months and 12 months post B-Laser™ device procedure compared to baseline. ○ Improved Grade of Walking Impairment Questionnaire (WIQ) at 30 days, 6 month and 12 months post B-Laser™ device procedure compared to baseline.

¹ Device/Procedure-related AE refers only to B-Laser™ atherectomy procedure and not the entire index procedure

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Inclusion Criteria	<ol style="list-style-type: none"> 1. Subject is ≥ 18 years old. 2. Subject is a candidate for endovascular intervention for PAD in the lower extremities. 3. Documented symptomatic atherosclerotic PAD Rutherford Classification 2-4. 4. Subject has infrainguinal target lesion(s) with any type of stenosis (naïve or recurrent) estimated to be $\geq 70\%$ based on CT angiogram or other imaging modality. 5. At least one patent tibial run-off vessel at baseline. 6. Subject is capable and willing to comply with the scheduled follow up. 7. Subject is able and willing to sign a written informed consent form (ICF). <p>Intraoperative inclusion criteria (by fluoroscopy angiogram):</p> <ol style="list-style-type: none"> 1. Reference vessel lumen diameter proximal to target lesion is $\geq 150\%$ of the outer diameter of the B-Laser™ to be used. 2. Target lesion has been crossed with a guidewire within the true lumen. 3. Target lesion has a stenosis estimated to be $\geq 70\%$.
Exclusion Criteria	<ol style="list-style-type: none"> 1. Target lesion is in a vessel graft or synthetic graft. 2. Target lesion length >25 cm. 3. Endovascular or surgical procedure performed less than or equal to 30 days prior to index procedure OR Planned endovascular or surgical procedure 30 days post index procedure. 4. Intent to use other atherectomy device in the same procedure. 5. Flow limiting dissection proximal to, distal to or in the target lesion. 6. Evidence or history of intracranial or gastrointestinal bleeding, intracranial aneurysm, myocardial infarction or stroke within the past 2 months. 7. Evidence or history of aneurysm in the target vessel within the past 2 months. 8. History of bleeding diathesis, coagulopathy or inability to accept blood transfusions. 9. History of heparin-induced thrombocytopenia (HIT). 10. Significant acute or chronic kidney disease with a creatinine level >2.5 mg/dl, and/or requiring dialysis. 11. Any thrombolytic therapy within 2 weeks of the index procedure. 12. History of severe trauma, fracture, major surgery or biopsy of a parenchymal organ within the past 14 days. 13. Known allergy to contrast agents or medications used to perform endovascular intervention that cannot be adequately pre-treated. 14. Subjects in whom anti-platelet, anticoagulant, or thrombolytic therapy is contraindicated. 15. Serious illness that may affect subject compliance to protocol and at a minimum the 30-day follow-up. 16. Participating in other clinical study that involves any kind of intervention, including pharmaceutical. 17. Issue that in the judgment of the investigator, may affect the results of the study. 18. Subject is pregnant or planning to become pregnant during the study period. <p>Intraoperative exclusion criteria (by fluoroscopy angiogram):</p> <ol style="list-style-type: none"> 1. Total occlusion of the Target lesion that cannot be crossed in the true lumen by 0.014" GW. 2. Target lesion length >25 cm. 3. Reference vessel lumen diameter proximal to target lesion $<150\%$ of B-Laser™ diameter. 4. Any clinical and/or angiographic complication attributed to the use of another device prior to study procedure. 5. Flow limiting dissection proximal, distal or in the target lesion.

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Study Duration:	30 days post procedure for the primary endpoint and up to 12 months for the secondary endpoints for each subject. Therefore, total study expected duration is 15.5 months (3.5 m + 12 m follow-up).																																																																																			
Number of Subjects & Sample Size Calculation:	The sample size selected for this study may be between 20 to 60 treated subjects which are deemed appropriate to assess device safety, per primary safety endpoint of 30 days MAE rate, and with one-sided 95% exact binomial confidence interval to represent the reliability level of the estimated MAE rate and the claim for safety.																																																																																			
Clinical Sites:	Up to 4 recruiting centers, additional sites may be added according to recruitment rate.																																																																																			
Statistical Analysis:	<u>General:</u> Descriptive statistics will be presented per each visit basis. Study Populations: <u>Safety Analysis Set (SA):</u> consist of all subjects enrolled in the study, and underwent the study procedure with the investigational device. The SA set will serve as the main analysis set for safety analyses both primary and secondary. <u>Efficacy Analysis Set (EF):</u> consist of all subjects enrolled in the study, and underwent the study procedure with the investigational device, for which data is available regarding the primary efficacy endpoint and had no major protocol deviations. The EF set will serve as the main analysis set for all efficacy analyses.																																																																																			
Schedule of events:	<table><tr><th>Visit, Number, (Time point)</th><th>Screening Visit 1 (<2m pre-procedure)</th><th>B-Laser™ procedure Visit 2 (to discharge)</th><th>Follow up Visit 3 (30d ± 5d post procedure)</th><th>Follow up Visit 4 (6m ± 2w post procedure)</th><th>Follow up Visit 5 (12m ± 1m post procedure)</th></tr><tr><td>Informed consent</td><td>X</td><td></td><td></td><td></td><td></td></tr><tr><td>Assess eligibility</td><td>X</td><td></td><td></td><td></td><td></td></tr><tr><td>Medical history & demographic</td><td>X</td><td></td><td></td><td></td><td></td></tr><tr><td>Blood Tests</td><td>X</td><td></td><td></td><td></td><td></td></tr><tr><td>Con-meds</td><td>X</td><td>X</td><td>X</td><td>X</td><td>X</td></tr><tr><td>Baseline lesion evaluation</td><td>X</td><td>X</td><td></td><td></td><td></td></tr><tr><td>Short Physical examination</td><td>X</td><td></td><td></td><td></td><td></td></tr><tr><td>Ankle-Brachial Index</td><td>X</td><td></td><td>X</td><td>X</td><td>X</td></tr><tr><td>Rutherford Classification</td><td>X</td><td></td><td>X</td><td>X</td><td>X</td></tr><tr><td>WIQ</td><td>X</td><td></td><td>X</td><td>X</td><td>X</td></tr><tr><td>PAD Intervention including B-Laser™ Atherectomy</td><td></td><td>X</td><td></td><td></td><td></td></tr><tr><td>Safety- AE, SAE, MAE, ADE</td><td></td><td>X</td><td>X</td><td>X</td><td>X</td></tr></table>						Visit, Number, (Time point)	Screening Visit 1 (<2m pre-procedure)	B-Laser™ procedure Visit 2 (to discharge)	Follow up Visit 3 (30d ± 5d post procedure)	Follow up Visit 4 (6m ± 2w post procedure)	Follow up Visit 5 (12m ± 1m post procedure)	Informed consent	X					Assess eligibility	X					Medical history & demographic	X					Blood Tests	X					Con-meds	X	X	X	X	X	Baseline lesion evaluation	X	X				Short Physical examination	X					Ankle-Brachial Index	X		X	X	X	Rutherford Classification	X		X	X	X	WIQ	X		X	X	X	PAD Intervention including B-Laser™ Atherectomy		X				Safety- AE, SAE, MAE, ADE		X	X	X	X
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