

## Attachment A1 – Clinical Study Definitions

**ABI** - Ankle-brachial index. Ankle systolic pressure/brachial systolic pressure. 0.9-1.2 = normal, < 0.9 = peripheral arterial disease, < 0.4 = severe peripheral arterial disease (ischemic pain and ulceration). ABI > 1.2 is likely due to incompressible arteries and is commonly observed in association with long-standing diabetes mellitus, extreme old age, or calcinosis.

**ABI, Exercise** - ABI measured one minute post-exercise at 3.5 km/hr and 12% grade for five minutes or until symptoms develop. Abnormal exercise ABI is defined as a drop of  $\geq 25\%$  from resting ABI.

**Above-the-knee Femoropopliteal Artery** - Includes the SFA (located below the bifurcation from the external iliac artery) and the popliteal artery above the plane of the femoral epicondyles. **To avoid involvement of the common femoral artery, the proximal end of the stent should be placed at least 1 cm below the origin of the bifurcation into the SFA. To avoid involvement of the below-the-knee popliteal artery, the distal end of the stent should be placed above the plane of the femoral epicondyles.**

**Adverse Event, Major (MAE)** - Includes death, target lesion revascularization (see definition of “target lesion revascularization (TLR)”), target limb ischemia requiring surgical intervention (bypass or amputation of toe, foot, or leg), and surgical repair of the target vessel (e.g., vessel dissection or perforation requiring surgery).

**Adverse Event, Early** - Clinical events that occur within 30 days (< 30 days) of the procedure.

**Adverse Event, Late** - Clinical events that occur 30 or more days ( $\geq 30$  days) after the procedure.

**Anaphylaxis** - Any allergic reaction following the introduction of a substance, that is characterized by dyspnea, clinically significant hypotension, shock, angioedema, dermal eruption, generalized urticaria, and/or death.

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***Blue Toe Syndrome (atheroembolization)*** - Atherothrombotic microembolism of the lower extremities with painful cyanotic discoloration of the toes.

***Blood Chemistry*** - Venous blood evaluation (SMA-12).

***Classification of Lesion Morphology (TASC):***

**Type A Femoropopliteal Lesions** - Single stenosis up to 3 cm in length, not at the origin of the SFA or the distal popliteal artery.

**Type B Femoropopliteal Lesions** - Single stenoses or occlusions 3-5 cm long, not involving the distal popliteal artery; heavily calcified stenoses up to 3 cm in length; multiple lesions, each less than 3 cm (stenoses or occlusions); single or multiple lesions in the absence of continuous tibial runoff to improve inflow for distal surgical bypass.

**Type C Femoropopliteal Lesions** - Single stenosis or occlusion longer than 5 cm; multiple stenoses or occlusions, each 3-5 cm, with or without heavy calcification.

**Type D Femoropopliteal Lesions** - Complete common femoral artery or SFA occlusions or complete popliteal and proximal trifurcation occlusions.

***Critical Limb Ischemia (CLI)*** - A Rutherford score of 4-6.

***Dissection Grades:***

**A** - Small radiolucent area within the lumen of the vessel disappearing with the passage of the contrast material.

**B** - Filling defect parallel to the lumen of the vessel disappearing with the passage of contrast material.

**C** - Dissection protruding outside the lumen of the vessel persisting after passage of contrast material.

**D** - Spiral shaped filling defect with delayed runoff of the contrast material in the distal vessel.

**E** - Persistent luminal filling defect with delayed antegrade flow.

**F** - Filling defect accompanied by total occlusion.

***Event-free Survival*** - Freedom from the CEC-adjudicated major adverse events (Adverse Events, Major; see definition) including worsening of the Rutherford classification by 2 classes or to class 5 or 6. Failure of event-free survival occurs when a) the CEC adjudicates a major adverse event as device and/or procedure related, b) the CEC

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adjudicates a revascularization as clinically driven target lesion failure (i.e., TLR), or c) the Rutherford classification worsens by 2 classes or to class 5 or 6.

***EQ-5D*** - A self-administrated, health-related quality of life measure including the following five dimensions: mobility, self care, usual activities, pain/discomfort, anxiety/depression.

***Failure, Procedural*** - Vessel with  $\geq 30\%$  residual stenosis determined angiographically immediately after the procedure.

***Hematoma/Hemorrhage*** - A localized collection of blood, usually clotted, in an organ, space, or tissue, due to a break in the wall of a blood vessel; bleeding into an extravascular space, which could be outside the body. A serious adverse event hematoma or hemorrhage is one requiring transfusion, surgical intervention, or causing death.

***Infection of Access Site*** - Typically presents with erythema, edema, heat, pain, tenderness, and purulent discharge. (Note: cultures of the wound are not required.)

***Limb Loss*** - Amputation of a leg, either above the knee or below the knee, including amputation of the foot or toes.

***Minimum Lumen Diameter (MLD)*** - Mean minimum lumen diameter (mm) from 2 orthogonal views.

***Myocardial Infarction (Non-Q-Wave)*** - Clinical evidence of elevated peak CK values greater than three times the upper limit of normal with elevated CK-MB fraction (above the institution's upper limit of normal) in the absence of new pathological Q-waves.

***Myocardial Infarction (Q-Wave)*** - Post-procedure presence of new Q-waves greater than 0.04 seconds in 2 contiguous leads with elevation of CK greater than three times the upper limit of normal and MB fraction greater than the upper limit of normal.

***New York Heart Association Classification:***

**Class I** - The patient has cardiac disease but without resulting limitations of ordinary physical activity. Ordinary physical activity (i.e., walking several blocks or climbing

stairs) does not cause undue fatigue, palpitation, dyspnea, or anginal pain. Limiting symptoms may occur with marked exertion.

**Class II** - The patient has cardiac disease resulting in slight limitation of ordinary physical activity. Patient is comfortable at rest. Ordinary physical activity such as walking more than two blocks or climbing more than one flight of stairs results in limiting symptoms (e.g., fatigue, palpitation, dyspnea, or anginal pain).

**Class III** - The patient has cardiac disease resulting in marked limitation of physical activity. Patient is comfortable at rest. Less than ordinary physical activity (i.e., walking one to two blocks or climbing one flight of stairs) causes fatigue, palpitation, dyspnea, or anginal pain.

**Class IV** - The patient has dyspnea at rest that increases with any physical activity. Patient has cardiac disease resulting in inability to perform any physical activity without discomfort. Symptoms of cardiac insufficiency or anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

**Occlusion** - No flow identified within the arterial segment by ultrasound and/or angiogram.

**Patency** - A demonstrably open treated segment (i.e., < 50% diameter stenosis, including the region within  $\pm$  5 mm proximal and/or distal to the target lesion) as assessed via duplex ultrasound (PSV < 2.0) and/or angiography (note: in cases where both imaging modalities are available, the angiography will take precedence).

**Patency Rate, Primary** - The proportion of treated segments with uninterrupted (intervention-free) patency (i.e., < 50% diameter stenosis) since the initial procedure. Failure of primary patency occurs at the first occurrence of one of the following: acute PTA failure, loss of patency (i.e.,  $\geq$  50% diameter stenosis, including the region within  $\pm$  5 mm proximal and/or distal to the study segment, as assessed via ultrasound (PSV  $\geq$  2.0) and/or angiography; in cases where both imaging modalities are available, the angiography will take precedence), reintervention in the study segment due to  $\geq$  50% angiographic diameter stenosis, total occlusion of the treated segment, surgical bypass due to treated segment restenosis (see definition), or amputation of the extremity due to treated segment restenosis (see definition).

**Patency Rate, Assisted Primary** - The proportion of target lesions that are successfully opened at the initial procedure, but that subsequently requires an intervention to assist

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patency maintenance of the target lesion, without an episode of total occlusion. Failure of primary assisted patency occurs at the time of one of the following: total occlusion of the target lesion, surgical bypass of the target lesion, or amputation of the extremity due to target lesion restenosis.

***Patency Rate, Secondary*** - The proportion of target lesions that are successfully opened at the initial procedure, but that subsequently becomes totally occluded and is then successfully re-opened in a secondary procedure. Failure of secondary patency occurs at the time of one of the following: surgical bypass of the target lesion or amputation of the extremity due to target lesion restenosis.

***Percent Diameter Stenosis (%DS)*** -  $100 \times (1 - (\text{MLD}/\text{RVD}))$ , where MLD = minimum lumen diameter and RVD = reference vessel diameter.

***PSV Ratio*** - The ratio of the peak systolic velocity (PSV) in the target lesion to that of the proximal reference vessel.

***PTA Failure, Acute*** - One or more of the following documented at the time of the procedure:

- a) an inadequate angiographic and/or hemodynamic result as defined by a 30% or greater diameter stenosis (the stenosis may be due to residual stenosis, recoil, dissection, or intimal flaps, for example);
- b) a 5 mmHg or greater mean trans-stenotic pressure gradient measured with a pressure wire or  $\leq 4$  Fr catheter; or
- c) acute occlusion of the vessel.

***PTA Failure, Long-term*** -  $\geq 50\%$  diameter stenosis including the region within  $\pm 5$  mm proximal and/or distal to the target lesion within 12 months of the index PTA procedure, confirmed and documented by duplex ultrasound or angiography.

***Quality of Life Questionnaire (QOL)*** - A standardized instrument for assessing patients' health status.

***Quantitative Angiography*** - A quantitative estimate obtained with a digital angiographic computer.

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**Reference Vessel Diameter, Proximal ( $RVD_{prox}$ )** - Diameter of normal segment immediately proximal to the treated region.

**Reference Vessel Diameter, Distal ( $RVD_{dist}$ )** - Diameter of normal segment immediately distal to the treated region.

**Renal Failure** - Acute or progressive renal insufficiency leading to the need for dialysis.

**Renal Insufficiency** - A rise in creatinine of more than 30% above the pre-procedure level resulting in a creatinine level  $> 2.0$  mg/dl that does not spontaneously resolve.

**Restenosis** - Recurrence of  $\geq 50\%$  diameter stenosis within  $\pm 5$  mm proximal and/or distal to the target lesion as measured by duplex ultrasound ( $PSV \geq 2.0$ ) or angiography (note: in cases where both imaging modalities are available, the angiography will take precedence).

***Rutherford Categories:***

Class 0 - Asymptomatic, no hemodynamically significant occlusive disease.

Class 1 - Mild claudication.

Class 2 - Moderate claudication.

Class 3 - Severe claudication.

Class 4 - Ischemic rest pain.

Class 5 - Minor tissue loss.

Class 6 - Major tissue loss.

***Stent Strut Fracture Types<sup>[8]</sup>:***

Type 0 - No strut fractures.

Type I - Single strut fracture only.

Type II - Multiple single strut fractures that can occur at different sites.

Type III - Multiple strut fractures resulting in complete transection of the stent, without displacement of the stent segments.

Type IV - Multiple strut fractures resulting in displacement of segments of the stent\*.

\*Note: Type IV includes spiral fractures that could result in stent displacement without complete transection.

***Superficial Femoral Artery (SFA)*** - Terminal branch of the common femoral artery with the profunda femoris artery which passes down the anteromedial portion of the thigh through the femoral triangle to the opening in the adductor magnus muscle (adductor hiatus) where it becomes the popliteal artery.

***Success, Clinical*** - Patient must be improved by at least two Rutherford classes above the pretreatment clinical level at follow-up.

***Success, Procedural*** - Vessel with < 30% residual stenosis determined angiographically immediately after the procedure.

***Symptoms of PAD*** - Include but are not limited to: claudication (leg or hip pain during walking which stops when at rest), numbness, tingling or weakness in the legs, burning or aching pain in feet or toes at rest, sore on leg or foot that will not heal, cold legs or feet, color change in skin of legs or feet, or loss of hair on legs.

***Target Lesion Revascularization (TLR)*** - A reintervention performed for  $\geq 50\%$  diameter stenosis (confirmed by angiography) within  $\pm 5$  mm proximal and/or distal to the target lesion after documentation of recurrent clinical symptoms of PAD following the initial procedure.

***TBI*** - Toe-brachial index. Toe systolic pressure/brachial systolic pressure.  
 $\geq 0.8$  = normal,  $< 0.8$  = peripheral arterial disease.

***Thrombosis, Acute*** - Ultrasound, angiographic, or clinically proven complete occlusion of an artery occurring within 24 hours ( $< 24$  hours) of the procedure.

***Thrombosis, Subacute*** - Ultrasound, angiographic, or clinically proven complete occlusion of an artery occurring after 24 hours, but within 30 days of the procedure ( $\geq 24$  hours and  $< 30$  days).

***Thrombosis, Late*** - Ultrasound, angiographic, or clinically proven complete occlusion of an artery occurring 30 days or more ( $\geq 30$  days) after the procedure.

***Thrombosis, Intraluminal*** - Subtotal occlusion of the artery due to the presence of thrombus.

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***Ultrasound, Not Interpretable*** - An ultrasound with all of the following conditions:

1. PSV Ratio < 2;
2. The ultrasound waveform has degraded from the immediate post-procedural ultrasound (e.g., biphasic to monophasic); or
3. A lesion other than the target lesion cannot specifically be identified as the cause of the degradation.

***Walking Impairment Questionnaire (WIQ)*** - A measure of patient-perceived walking performance for patients with PAD and/or intermittent claudication. This questionnaire estimates walking distance, walking speed, and stair-climbing capacity. Improvement is defined as an increase of walking distance. (Hiatt WR, Hirsh AT, Regensteiner JG, Brass EP, and the Vascular Clinical Trialists. Clinical trials for claudication: assessment of exercise performance, functional status, and clinical end points. *Circulation*. 1995;92:614-621.)

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