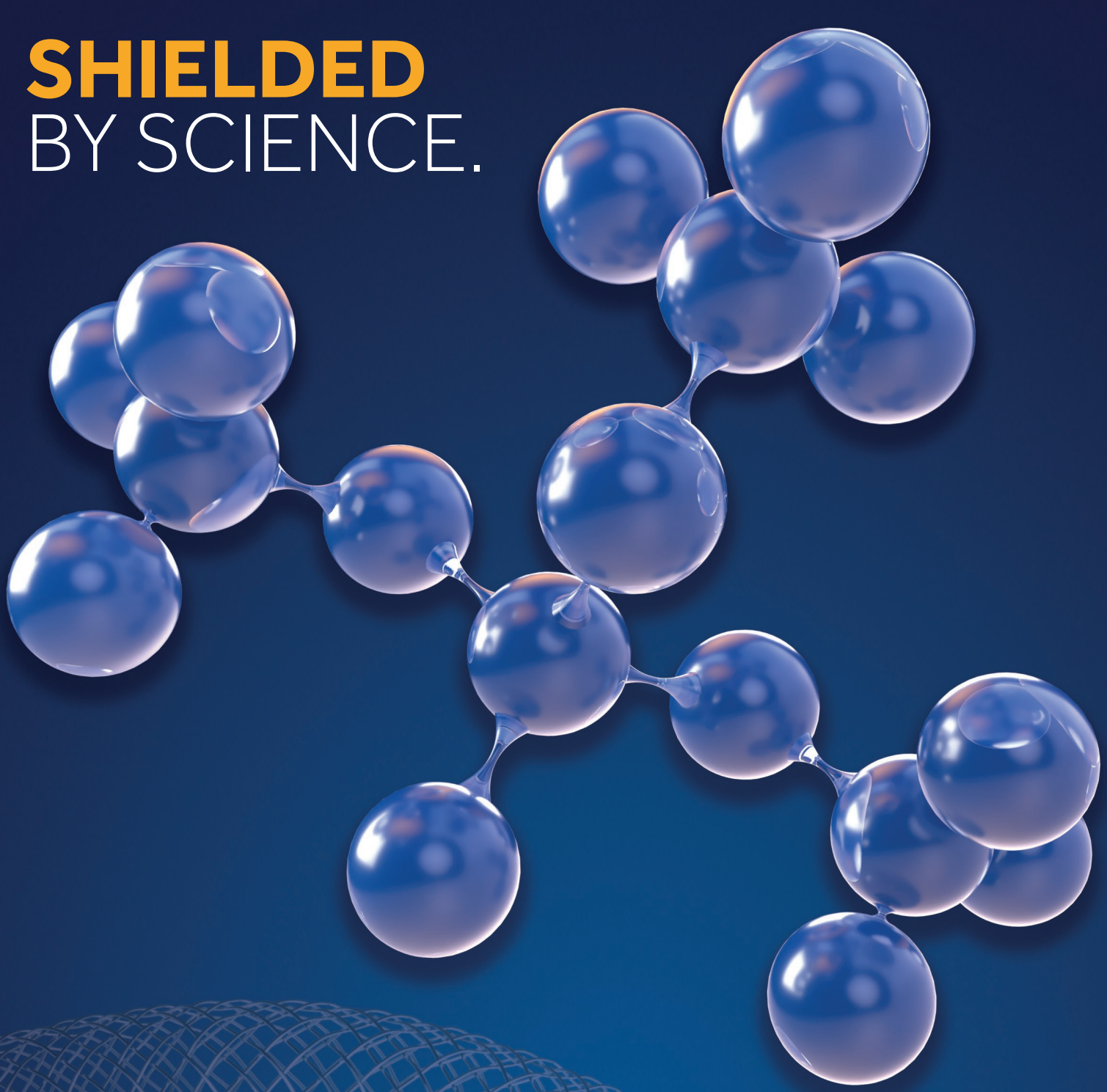
SHIELDED
BY SCIENCE.



Pipeline™ Flex

Embolization Device
with Shield Technology™

Medtronic

REDUCES **MATERIAL THROMBOGENICITY**[1,2*]

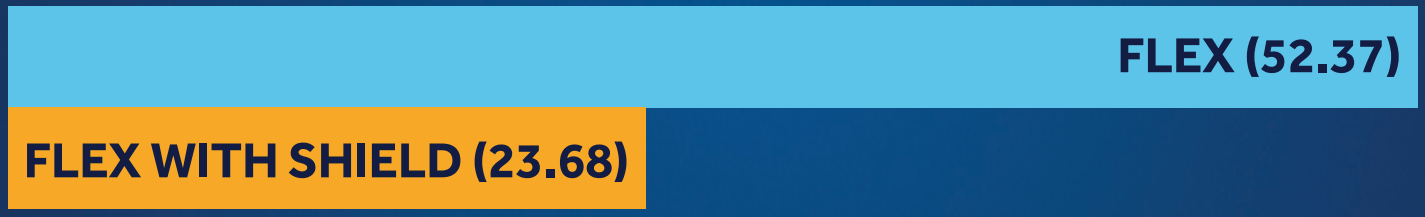
To advance flow diversion therapy, **Shield Technology**™ addresses one of its common barriers: material thrombogenicity.

Through covalently bonding phosphorylcholine to the surface of the implant, Shield Technology™ enhances the **Pipeline**™ **Flex** embolization device to achieve a scientifically proven reduction in implant material thrombogenicity as shown through in-vitro studies.[1,2*]

Human Blood Loop Model Results[1*]

94% reduction in platelet activation[1*]

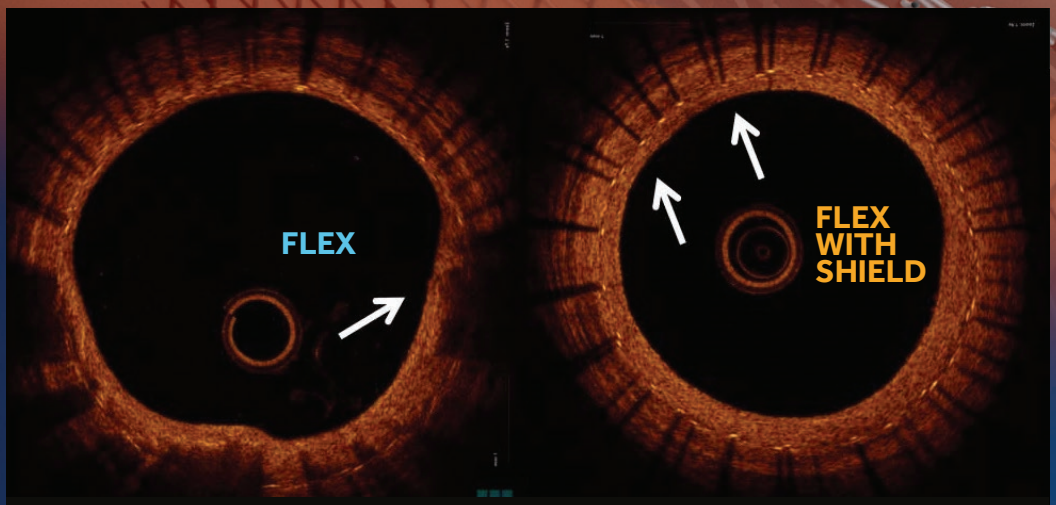
Mean Peak Thrombin (nM)[2*]



55% reduction in peak thrombin[2*]

* Data is derived from the referenced bench studies and may not be representative of clinical performance.

PROMOTES **ENDOTHELIALIZATION**[3,4*]

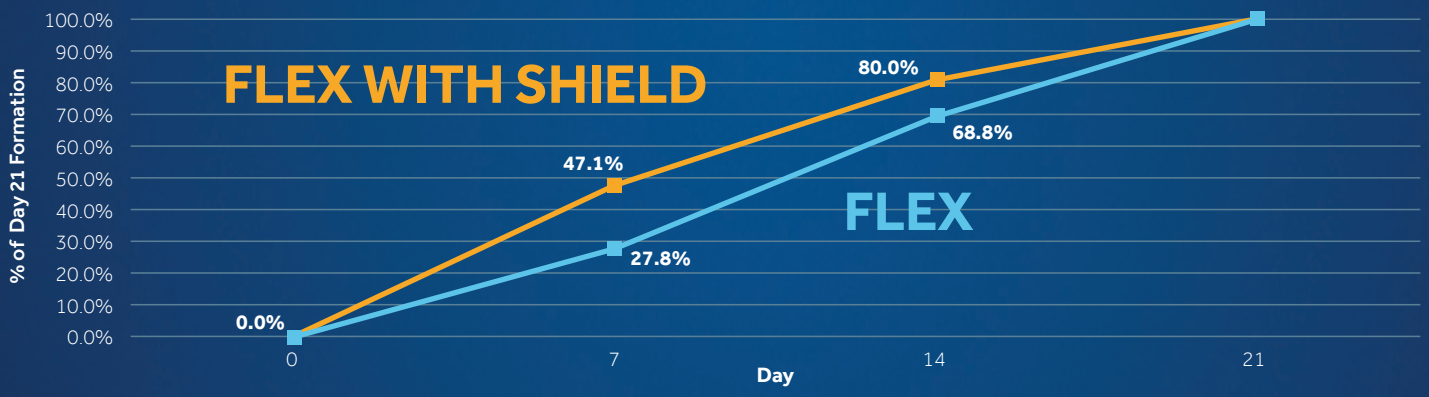


Analysis with Optical Coherence Tomography shows that the Pipeline™ Flex device with Shield Technology™ demonstrates a homogenous and concentric tissue response.[3*]

In-vivo testing shows that **Shield Technology**™ led to earlier and more even neointima formation[3*] with less hyperplasia and comparable aneurysm occlusion rates as the Pipeline™ Flex embolization device.[4*]

Neointima Thickness Ratio at Day 21[3*]

Neointima Formation over Time[3*]



* Data is derived from the referenced animal studies and may not be representative of clinical performance.

IMPROVES **PERFORMANCE**[5*]

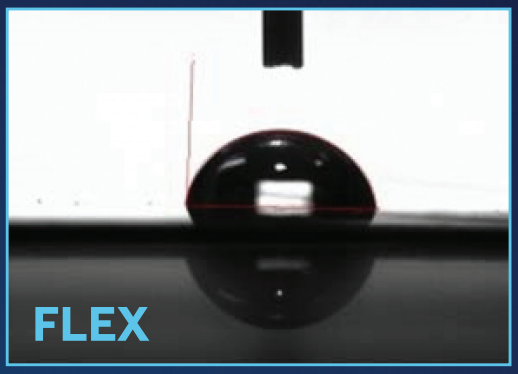
Shield Technology™ improves the customer experience through improvements in delivery and resheathing force through tortuousity.[5*]

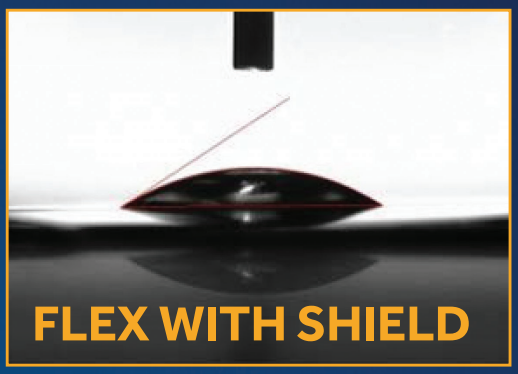
Delivery Force (N)

FLEX (PED-400-35)	**6.5**
FLEX WITH SHIELD (PED2-400-35)	**5.2**

Resheathing Force (N)

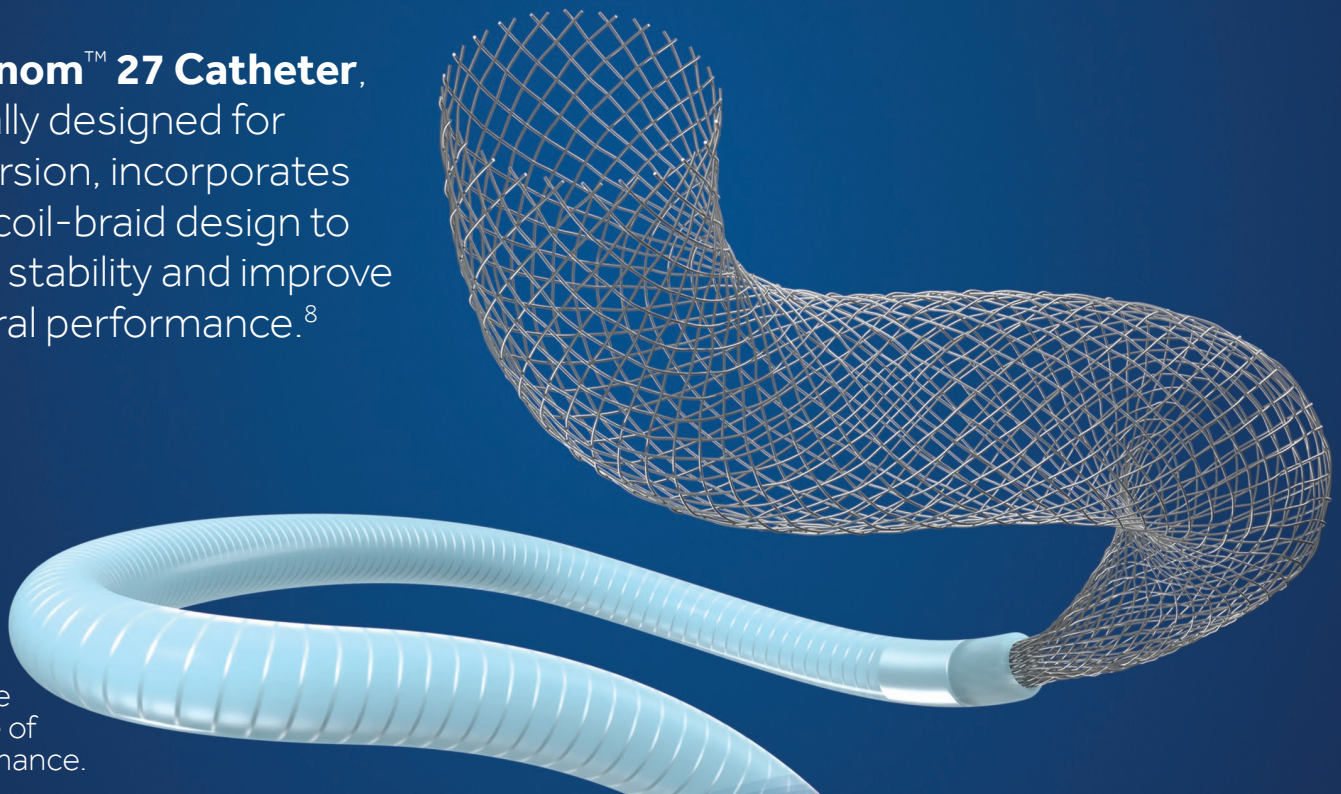
FLEX (PED-400-35)	**2.4**
FLEX WITH SHIELD (PED2-400-35)	**2.1**





The modified surface of the implant exhibits hydrophilic properties, decreasing delivery and resheathing forces by **20%** and **12%** respectively.[5*]

The **Phenom**™ **27 Catheter**, specifically designed for flow diversion, incorporates a hybrid coil-braid design to maintain stability and improve procedural performance.[8]



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PIPELINE™ FLEX EMBOLIZATION DEVICE

A clinically proven, cobalt-chromium and platinum-tungsten flow diversion device that's resheathable and redeployable.

PUFS Study Results[6*]

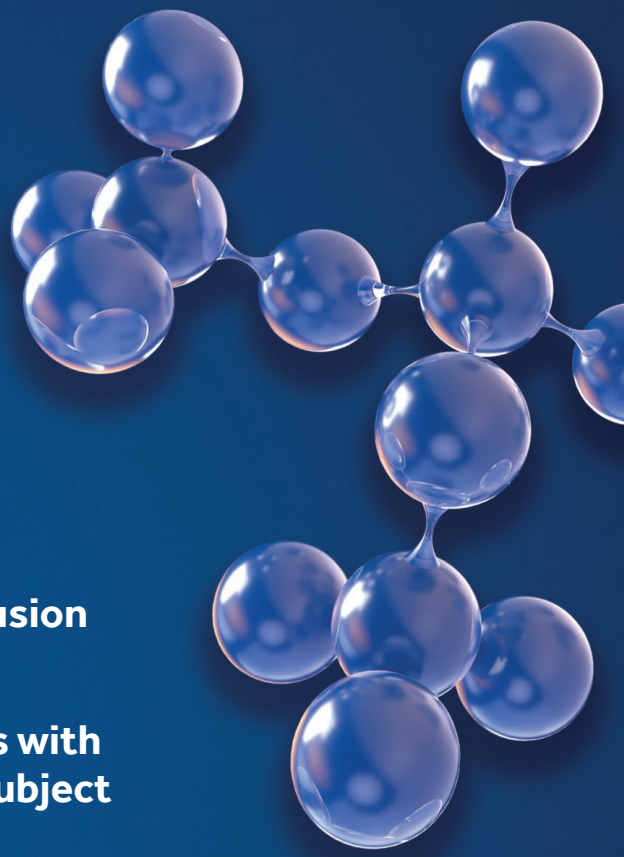
95%
Occlusion at 5 year follow-up

0%
Recurrence at 5 years after initial occlusion

* The PUFS study only included the Pipeline™ embolization device. The Pipeline™ Flex embolization device contains the same implant as the Pipeline™ embolization device.

NOW **SHIELDED** BY SCIENCE.

PFLEX and SHIELD Combined Results: Wide-Necked ICA Population[7]



3.1% **Primary Safety Endpoint***

75.7% **Primary Efficacy Endpoint** with 79.2% Complete Occlusion****

98.1% **Device Deployment Success with Average 1.1 Deployed per Subject**

* Primary Safety Endpoint defined as major stroke in the territory supplied by the treated artery or neurologic death through 1-year post-procedure.

** Primary Efficacy Endpoint defined as complete aneurysm occlusion without significant parent artery stenosis (≤50%) or retreatment of the target aneurysm through 1-year post procedure.

Diameter (mm)	Length (mm)	Reference Number
2.5	10	PED2-250-10
2.5	12	PED2-250-12
2.5	14	PED2-250-14
2.5	16	PED2-250-16
2.5	18	PED2-250-18
2.5	20	PED2-250-20
2.75	10	PED2-275-10
2.75	12	PED2-275-12
2.75	14	PED2-275-14
2.75	16	PED2-275-16
2.75	18	PED2-275-18
2.75	20	PED2-275-20
3.0	10	PED2-300-10
3.0	12	PED2-300-12
3.0	14	PED2-300-14
3.0	16	PED2-300-16
3.0	18	PED2-300-18
3.0	20	PED2-300-20
3.0	25	PED2-300-25
3.0	30	PED2-300-30
3.0	35	PED2-300-35
3.25	10	PED2-325-10
3.25	12	PED2-325-12
3.25	14	PED2-325-14
3.25	16	PED2-325-16
3.25	18	PED2-325-18
3.25	20	PED2-325-20
3.25	25	PED2-325-25
3.25	30	PED2-325-30
3.25	35	PED2-325-35
3.5	10	PED2-350-10
3.5	12	PED2-350-12
3.5	14	PED2-350-14
3.5	16	PED2-350-16
3.5	18	PED2-350-18
3.5	20	PED2-350-20
3.5	25	PED2-350-25
3.5	30	PED2-350-30
3.5	35	PED2-350-35
3.75	10	PED2-375-10
3.75	12	PED2-375-12
3.75	14	PED2-375-14
3.75	16	PED2-375-16
3.75	18	PED2-375-18
3.75	20	PED2-375-20
3.75	25	PED2-375-25
3.75	30	PED2-375-30
3.75	35	PED2-375-35
4.0	10	PED2-400-10
4.0	12	PED2-400-12
4.0	14	PED2-400-14
4.0	16	PED2-400-16
4.0	18	PED2-400-18
4.0	20	PED2-400-20
4.0	25	PED2-400-25
4.0	30	PED2-400-30
4.0	35	PED2-400-35
4.25	10	PED2-425-10
4.25	12	PED2-425-12
4.25	14	PED2-425-14
4.25	16	PED2-425-16
4.25	18	PED2-425-18
4.25	20	PED2-425-20
4.25	25	PED2-425-25
4.25	30	PED2-425-30
4.25	35	PED2-425-35
4.5	10	PED2-450-10
4.5	12	PED2-450-12
4.5	14	PED2-450-14
4.5	16	PED2-450-16
4.5	18	PED2-450-18
4.5	20	PED2-450-20
4.5	25	PED2-450-25
4.5	30	PED2-450-30
4.5	35	PED2-450-35
4.75	10	PED2-475-10
4.75	12	PED2-475-12
4.75	14	PED2-475-14
4.75	16	PED2-475-16
4.75	18	PED2-475-18
4.75	20	PED2-475-20
4.75	25	PED2-475-25
4.75	30	PED2-475-30
4.75	35	PED2-475-35
5.0	10	PED2-500-10
5.0	12	PED2-500-12
5.0	14	PED2-500-14
5.0	16	PED2-500-16
5.0	18	PED2-500-18
5.0	20	PED2-500-20
5.0	25	PED2-500-25
5.0	30	PED2-500-30
5.0	35	PED2-500-35

PIPELINE™ FLEX EMBOLIZATION DEVICE WITH SHIELD TECHNOLOGY™ ESSENTIAL PRESCRIBING INFORMATION (EPI) STATEMENT: CAUTION: Federal (USA) law restricts this device to sale, distribution and use by or on the order of a physician. Indications, contraindications, warnings and instructions for use for the Pipeline™ Flex Embolization Device with Shield Technology™ can be viewed at https://www.medtronic.com/manuals. **Indications for Use:** The Pipeline™ Flex Embolization Device with Shield Technology™ is indicated for the endovascular treatment of adults (22 years of age or older) with large or giant wide-necked intracranial aneurysms (IAs) in the internal carotid artery from the petrous to the superior hypophyseal segments. The Pipeline™ Flex Embolization Device with Shield Technology™ is also indicated for use in the internal carotid artery up to the terminus for the endovascular treatment of adults (22 years of age or older) with small and medium wide-necked (neck width ≥ 4 mm or dome-to-neck ratio < 2) saccular or fusiform intracranial aneurysm (IAs) arising from a parent vessel with a diameter ≥ 2.0 mm and ≤ 5.0 mm. **Contraindications**: 1) Patients with active bacterial infection. 2) Patients in whom dual antiplatelet and/or anticoagulation therapy (aspirin and clopidogrel) is contraindicated. 3) Patients who have not received dual antiplatelet agents prior to the procedure. 4) Patients in whom a pre-existing stent is in place in the parent artery at the target aneurysm location. 5) Patients in whom the parent vessel size does not fall within the indicated range. **Warnings:** 1) Pushing delivery wire without retracting the micro catheter at the same time will cause the open end braid to move distally in the vessel. This may cause damage to the braid or vessel. 2) Use in tortuous anatomy may result in difficulty or inability to deploy the Pipeline™ Flex Embolization Device with Shield Technology™ and can lead to damage to the Pipeline™ Flex Embolization Device with Shield Technology™ and microcatheter. To mitigate potential problems as a result of increased delivery forces, reduce the load in the system by: Unloading the microcatheter to the inner curves of vessel by pulling back on the system (i.e., the microcatheter and delivery wire together). Continue unloading the system until advancement of the device (inside the microcatheter) is observed, while minimizing the distal tip movement to prevent loss of position. Begin to re-advance the delivery wire while maintaining reduced load in the microcatheter. This process should be repeated until the device passes through tortuous area and the delivery force is decreased. 3) Resheathing of the Pipeline™ Flex Embolization Device with Shield Technology™ more than 2 full cycles may cause damage to the distal or proximal ends of the braid. 4) Persons with known allergy to platinum or cobalt/chromium alloy (including the major elements platinum, cobalt, chromium, nickel, molybdenum or tungsten) may suffer an allergic reaction to the Pipeline™ Flex Embolization Device with Shield Technology™ implant. 5) Person with known allergy to tin, silver, stainless steel, or silicone elastomer may suffer an allergic reaction to the Pipeline™ Flex Embolization Device with Shield Technology™ delivery system. 6) Do not reprocess or resterilize. Reprocessing and resterilization increase the risk of patient infection and compromised device performance. 7) Post-procedural movement (migration and/or foreshortening) of the Pipeline™ Flex Embolization Device with Shield Technology™ implant may occur following implantation and can result in serious adverse events and/or death. 8) Factors which may contribute to post procedural device movement include (but are not limited to) the following: Failure to adequately size the implant (i.e., under sizing), Failure to obtain adequate wall apposition during the implant deployment, Implant stretching, Vasospasm, Severe vessel tapering, Tortuous anatomy 9) Delayed rupture may occur with large and giant aneurysms. 10) Placement of multiple Pipeline™ Flex Embolization Device with Shield Technology™ may increase the risk of ischemic complications. 11) Use in anatomy with severe tortuosity, stenosis or parent vessel narrowing may result in difficulty or inability to deploy the Pipeline™ Flex Embolization Device with Shield Technology™ and can lead to damage to the Pipeline™ Flex Embolization Device with Shield Technology™ and microcatheter. Advancement or retraction of the Pipeline™ Flex Embolization Device with Shield Technology™ against resistance may result in damage, including unintended device or component separation, fracture, or breakage of the delivery system due to inherent flexibility limits of device design. Device damage may result in patient injury or death. Refer to page 4 in the instructions for use for additional information. 12) Do not attempt to reposition the device after full deployment. 13) The benefits may not outweigh the risks of treatment of small and medium asymptomatic extradural intracranial aneurysms, including those located in the cavernous internal carotid artery. The risk of rupture for small and medium asymptomatic extradural intracranial aneurysms is very low if not negligible. 14) A decrease in the proportion of patients who achieve complete aneurysm occlusion without significant parent artery stenosis has been observed with the use of the device in the communicating segment (C7) of the internal carotid artery (47.4% (9/19 subjects in the PREMIER study at 1 year)), including those IAs fed by the posterior circulation or have retrograde filling. Ensure appropriate patient selection and weigh the benefits and risks of alternative treatments prior to use of this device for the treatment of intracranial aneurysms located in this region of the ICA. The following anatomical characteristics, associated with retrograde filling, should be carefully considered during procedural planning of C7 intracranial aneurysms: PComm of fetal origin (A PCA of fetal origin is defined as a small, hypoplastic, or absent P1 segment of the PCA with the PComm artery supplying a majority of blood flow to the ICA); PComm overlapping with the aneurysm neck; and/or PComm branch arising from the dome of the aneurysm. 15) The safety and effectiveness of this device for radial neurovasculature access in direct comparison to a transfemoral approach has not been demonstrated. The risks and benefits for radial access against a transfemoral approach should be carefully weighed and considered for each patient. **Precautions:** 1) The Pipeline™ Flex Embolization Device with Shield Technology™ should be used only by physicians trained in percutaneous, intravascular techniques, and procedures at medical facilities with the appropriate fluoroscopy equipment. 2) Physicians should undergo appropriate training prior to using the Pipeline™ Flex Embolization Device with Shield Technology™ in patients. 3) The Pipeline™ Flex Embolization Device with Shield Technology™ is intended for single use only. Store in a cool, dry place. Carefully inspect the sterile package and device components prior to use to verify that they have not been damaged during shipping. Do not use kinked or damaged components. Do not use product if the sterile package is damaged. 4) Use the Pipeline™ Flex Embolization Device with Shield Technology™ system prior to the "Use By" date printed on the package. 5) The appropriate anti-platelet and anti-coagulation therapy should be administered in accordance with standard medical practice. 6) A thrombosing aneurysm may aggravate pre-existing, or cause new, symptoms of mass effect and may require medical therapy. 7) Use of implants with labeled diameter larger than the parent vessel diameter may result in decreased effectiveness and additional safety risk due to incomplete foreshortening resulting in an implant longer than anticipated. 8) The Pipeline™ Flex Embolization Device with Shield Technology™ may create local field inhomogeneity and susceptibility artifacts during magnetic resonance angiography (MRA), which may degrade the diagnostic quality to assess effective intracranial aneurysm treatment. 9) Take all necessary precautions to limit X-radiation doses to patients and themselves by using sufficient shielding, reducing fluoroscopy times, and modifying X-ray technical factors where possible. 10) Carefully weigh the benefits of treatment vs. the risks associated with treatment using the device for each individual patient based on their medical health status and risks factors for intracranial aneurysm rupture during their expected life time such as age, medical comorbidities, history of smoking, intracranial aneurysm size, location, and morphology, family history, history of prior asymptomatic subarachnoid hemorrhage (aSAH), documented growth of intracranial aneurysm on serial imaging, presence of multiple intracranial aneurysms, and presence of concurrent pathology. The benefits of device use may not outweigh the risks associated with the device in certain patients; therefore, judicious patient selection is recommended. 11) The safety and effectiveness of the device has not been established for treatment of fusiform IAs. 12) There may be a decrease in effectiveness and increase in safety events when the device is used in patients ≥ 60 years old. 13) The safety and effectiveness of the device has not been evaluated or demonstrated for ruptured aneurysms. 14) If using radial artery access, perform a screening examination of the radial artery per institutional practices to ensure that radial access is appropriate for the patient. **Potential Complications:** Potential complications of the device and the endovascular procedure include, but are not limited to, the following: Access site complications like hematoma, inflammation, infection, necrosis, pain and tenderness, granuloma; Adverse reaction to anti-platelet/anticoagulation agents, anesthesia, reactions due to radiation exposure (such as alopecia, burns ranging in severity from skin reddening to ulcers, cataracts and delayed neoplasia) or contrast media, including organ failure; Vascular Complications like vasospasm, stenosis, dissection, perforation, rupture, fistula formation, pseudo aneurysm, occlusion, thromboembolic complications including ischemia (to unintended territory); Device complications like fracture, breakage (including unintended device or component separation), misplacement, migration/delayed foreshortening or reaction to device materials may occur; Systemic Complications like: Infection, Pain, fever, allergic reactions, organ failure, nerve damage; Bleeding/hemorrhagic complication including retroperitoneal hemorrhage; Neurological Deficits or dysfunctions including Stroke, Infarction, Loss of vision, Seizures, TIA, Headache, Cranial Nerve Palsies, Confusion, Coma, Hand Dysfunction; Decreased therapeutic response including need for target aneurysm retreatment; Risks associated with visual symptoms include Amaurosis Fugax/transient blindness, Blindness, Diplopia, Reduced visual acuity/field, Retinal artery occlusion, Retinal ischemia, Retinal infarction, Vision impairment including scintillations, blurred vision, eye floaters; Intracranial Hemorrhage (including from Aneurysm Rupture) Brain Edema, Hydrocephalus, Mass Effect; Death.

PHENOM™ CATHETER INDICATIONS FOR USE: The Phenom™ Catheters are intended for the introduction of interventional devices or diagnostic agents into the neuro, peripheral, and coronary vasculatures. **CAUTION:** Federal (USA) law restricts this device to sale, distribution and use by or on the order of a physician. Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.

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1. Medtronic Internal Study, D00422708 Rev. A, Competitive Test Report - Material Thrombogenicity Evaluation of Flow Diversion Devices. **2.** Girdhar G, Li J, Kostousov L, Wainwright J, Chandler WL. In-vitro thrombogenicity assessment of flow diversion and aneurysm bridging devices. J Thromb Thrombolysis. 2015 Nov;40(4):437-43. doi: 10.1007/s11239-015-1228-0. PMID: 25975924. **3.** Matsuda Y, Chung J, Lopes DKAnalysis of neointima development in flow diverters using optical coherence tomography imaging Journal of NeuroInterventional Surgery 2018;10:162-167. **4.** Caroff J, Tamura T, King RM, et al Phosphorylcholine surface modified flow diverter associated with reduced intimal hyperplasia Journal of NeuroInterventional Surgery 2018;10:1097-1101. **5.** Medtronic Internal Study, TR-NV11991 Rev. B, Performance Evaluation of the Pipeline Flex Embolization Device with Shield Technology. **6.** Becske T, Brinjikji W, Potts MB, Kallmes DF, Shapiro M, Moran CJ, Levy EI, McDougall CG, Szikora I, Lanzino G, Woo HH, Lopes DK, Siddiqui AH, Albuquerque FC, Fiorella DJ, Saatci I, Cekirge SH, Berez AL, Cher DJ, Berentei Z, Marosfoi M, Nelson PK. Long-Term Clinical and Angiographic Outcomes Following Pipeline Embolization Device Treatment of Complex Internal Carotid Artery Aneurysms: Five-Year Results of the Pipeline for Uncoilable or Failed Aneurysms Trial. Neurosurgery. 2017 Jan 1;80(1):40-48. doi: 10.1093/neuros/nyw014. PMID: 28362885. **7.** Medtronic Internal Study, D00220076 Rev. A: Integrated Analysis of Clinical Outcomes using Pipeline™ with and without the Shield Surface Modification. **8.** Medtronic Internal Study, TR-NV15405 Rev. A, Micro-Catheter Compatibility Verification of Pipeline Flex with Shield Technology