Summary of Safety and Clinical Performance (SSCP)

for the class III medical device group

Neurovascular Flow Diverter

consisting of

p64,

p48 MW (HPC), p64 MW (HPC)

and p48 LITE (HPC) Flow Modulation Devices

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Revision:	D
Basis for the set-up:	Medical Device Regulation (MDR 2017/745), Article 32 Medical Device Coordination Group Document 2019-9 - Rev.1
Basic UDI-DI:	426012378FlowDiverterSV

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Purpose of the summary report on safety and clinical performance

The purpose of the Summary of Safety and Clinical Performance (= SSCP) is to explain the most important information about the safety and clinical performance of the medical device group Neurovascular Flow Diverter to the reader, both healthcare professionals and patients or lay persons, in a comprehensible way. This report will help to ensure that the public has adequate access to information about the medical device group Neurovascular Flow Diverter.

The SSCP is not intended to provide general advice on the diagnosis or treatment of vascular diseases e.g., saccular and fusiform aneurysms nor to replace the Instructions for Use (IFUs) as the primary documents provided to ensure the safe use of the medical device group Neurovascular Flow Diverter, nor to replace the mandatory information on the implant cards.

This SSCP has been validated by the Notified Body DQS (see chapter 1.9) in English language. This version was used as the basis for translation into other EU languages. The SSCP is regularly updated in Eudamed.

Terms, abbreviations and definitions

Terms	Definition
ASA	Acetylsalicylic acid
Basic UDI-DI	Basic Unique Device Identification – Device Identifier. The Basic UDI-DI is a root category for a specific device family. Many UDI-DIs can be associated with one basic UDI-DI.
BfArM	The German Federal Institute for Drugs and Medical devices (German: Bundesinstitut für Arzneimittel und Medizinprodukte) is an organizationally independent higher federal authority with its headquarters in the city of Bonn/Germany.
CE-certification	The CE marking of a medical device shows its complete compliance with the legal requirements.
Clinical Evaluation	A Clinical Evaluation is a systematic collection and evaluation of clinical data from a wide variety of sources. The manufacturer is obliged to conduct a Clinical Evaluation during the entire life cycle of a medical device. Thus, a Clinical Evaluation also includes a clinical follow-up of the medical device in the market.
ClinicalTrials.gov	ClinicalTrials.gov is a clinical trials registry. It is operated by the United States National Library of Medicine at the National Institutes of Health and is the largest clinical trials database with registrations of over 329,000 trials from 209 countries.
CS	Common Specifications are a set of standards provided by European Commission that have to be applied by manufacturers where no or insufficient harmonized standards exist.
DQS	The DQS (Deutsche Gesellschaft zur Zertifizierung von Qualitätssicherungssystemen = German Association for the certification of quality assurance systems) is a Notified Body.
EMDN	European Medical Device Nomenclature (EMDN Code) is the nomenclature that is used by the manufacturers when registering their Medical Devices in the Eudamed database.
Eudamed	European Database on Medical Devices (https://ec.europa.eu/tools/eudamed) - Eudamed will provide a living picture of the lifecycle of medical devices that are made available in the European Union (EU). Eudamed aims to enhance overall transparency, including through better access to information for the public and healthcare professionals, and to enhance coordination between the different Member States in the EU.
FDA	Food and Drug Administration is a federal agency of the United States, that controls and supervises the safety of food, tobacco, and medical products.
FDA-MAUDE	The Food and Drug Administration-Manufacturer and User Facility Experience is a website by the FDA

Terms	Definition
	(https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/search.cfm) where Manufacturers and Users can report issues regarding specific products.
FSCA	A Field Safety Corrective Action is an action taken by a manufacturer to reduce a risk of death or serious deterioration in the state of health associated with the use of a medical device that is already placed on the market. Such actions should be notified via a field safety notice.
FSN	A Field Safety Notice is a communication sent by a manufacturer to users or customers in relation to a corrective action taken by the manufacturer to prevent or reduce the risk of a serious incident.
GSPR	Manufacturers of medical devices have to establish conformity with the General Safety and Performance Requirements and should provide sufficient evidence to demonstrate compliance with GSPR.
HPC	Hydophilic Polymer Coating
IFU	Instructions For Use
Legacy Device	A medical device that was approved by a Notified Body under the so-called Medical Device Directive (MDD) and can be placed on the market without being newly CE-certified according to Medical Device Regulation (MDR) during a limited transition period.
MDD	Medical Device Directive (93/42/EEC) The MDD was the most important regulatory instrument for demonstrating the safety and medical-technical performance of medical devices in the European Economic Area until the Medical Device Regulation was introduced.
MDR	Medical Device Regulation (Regulation (EU) 2017/745). This Regulation covers the placing on the market, making available on the market and putting into service of medical devices and accessories intended for human use.
MRA	Mutual recognition agreements MRAs are trade agreements that aim to facilitate market access and encourage greater international harmonization of compliance standards while protecting consumer safety.
mRS	The modified Rankin Scale is a scale used to determine the degree of disability after a stroke. On this scale, 0 equals no symptoms after the stroke and 6 refers to death.
MW	Movabale Wire
NIHSS	National Institutes of Health Stroke Scale score
Notified Body	Notified Bodies of the European Union are officially designated and supervised authorities. The Notified Bodies ensure that uniform criteria related to a medical device are fulfilled throughout Europe (so-called conformity assessment procedure)
PMCF	The Post-Market Clinical Follow-Up is a systematic and proactive method of gathering clinical data on the safety and performance of CE-marked medical device.
PRRC	Person Responsible for Regulatory Compliance
SAH	Subarachnoid hemorrhage is bleeding in the space between the brain and the surrounding membrane (subarachnoid space).
SRN	A Single Registration Number is assigned to all medical device legal manufacturers, authorized representatives, system/procedure pack producers and importers involved in placing medical devices and in vitro diagnostics (IVD) on the European market. It is the primary means of identifying these so-called “Economic Operators” (EO) in the Eudamed database.
SSCP	Summary of Safety and Clinical Performance
Technical Documentation	The term Technical Documentation summarizes all information and documents that describe a product (such as a medical device) and explain its use and functionality. The Technical Documentation is understood as an essential part of the product.
TIA	Transient ischemic attack
UDI	The Unique Device Identification is a unique numeric or alphanumeric code for a medical device. It enables clear and unambiguous identification of certain products on the market and facilitates their traceability.
UDI-DI	Unique Device Identification – Device Identifier Every UDI-DI is associated with only one Basic UDI-DI.

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and p48 LITE (HPC) Flow Modulation Devices

Physicians and medical users and other healthcare professionals

Summary of safety and clinical performance for physicians and medical users and other healthcare professionals

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the medical device group Neurovascular Flow Diverter.

The SSCP is not intended to replace the Instructions For Use (IFU) as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.

The following information is intended for the physician and medical user of the medical device group Neurovascular Flow Diverter and other healthcare professionals.

1 Device identification and general information

1.1 Device trade name(s)

The medical device group Neurovascular Flow Diverter consists of the p64, p48 MW (HPC), p64 MW (HPC) and p48 LITE (HPC) Flow Modulation Devices (refer to Table 1). The product family p48 MW (HPC) consists of p48 MW and p48 MW HPC. This also applies to the p64 MW (HPC) and p48 LITE (HPC).The device versions with the suffix HPC carry a hydrophilic polymer coating.

Table 1: Classification of the medical device group Neurovascular Flow Diverter

Medical device group	Neurovascular Flow Diverter										
Basic UDI-DI	426012378FlowDiverterSV										
CE-certificate ID (Date of certification)	170781226 (21.12.2023)					1000236360 (28.08.2025)					
Product family	PAX-Flow Modulation Device										
Design variant	p64	p48 MW	p48 MW HPC	p64 MW	p64 MW HPC	p48 LITE	p48 LITE HPC	p48 MW*	p48 MW HPC*	p64 MW*	p64 MW HPC*
REF number: XX(X) – Model size	P64-XXX-XX	P48-MW-XXX-XX	P48-MW-HPC-XXX-XX	P64-MW-XXX-XX	P64-MW-HPC-XXX-XX	P48-LT-XXX-XX	P48-LT-HPC-XXX-XX	P48-MW-XXX- XX	P48-MW-HPC-XXX-XX	P64-MW-XXX -XX	P64-MW-HPC-XXX-XX

* harmonized delivery system

1.2 Manufacturer's name and address

phenox GmbH
Lise-Meitner-Allee 31
44801 Bochum

Germany
Tel.: +49 (0)234 36 919-0
Fax: +49 (0)234 36 919-19
E-Mail: info@wallabyphenox.com
Website: www.phenox.net

1.3 Manufacturer's single registration number (SRN)

The single registration number (SRN) is **DE-MF-000006524**.

1.4 Basic-UDI-DI (Product identification number)

The product identification number, also known as "Basic-UDI-DI" (Unique Device Identification - Device Identifier), is used to identify and register medical devices on the European Union market. The Basic-UDI-DI for the medical device group Neurovascular Flow Diverter is **426012378FlowDiverterSV**.

1.5 Medical device nomenclature description/text

According to the European Medical Device Nomenclature (MDR 2017/745, Article 26) (EMDN), the medical device group Neurovascular Flow Diverter belongs to the **"Vascular Stents" EMDN P070402**.

1.6 Class of device

The devices of the medical device group Neurovascular Flow Diverter are classified as Class III medical devices according to Annex VIII, Rule 8 Point 3 of the Medical Device Regulation (MDR) 2017/745.

1.7 Year when the first certificate (CE) was issued covering the device

- p64 was certified for the first time on 15.10.2012 (Certificate number: 506681 MRA acc. to MDD).
- p48 MW (HPC) was certified for the first time on 30.05.2018 (Certificate number: 539671 MRA acc. to MDD).
- p64 MW (HPC) certified for the first time on 22.12.2019 (Certificate number: 547128 MRA acc. to MDD).
- p64, p48 MW (HPC) and p64 MW (HPC) grouped under the medical device group Neurovascular Flow Diverter got CE-certified under MDR on 21.12.2023 (Certificate ID: 170781226).
- p48 LITE (HPC), p48 MW (HPC), and p64 MW (HPC) with harmonized guidance system got CE-certified under MDR on 28.08.2025 (Certificate ID: 1000236360).

1.8 Authorized representative if applicable; name and the SRN

Not applicable.

1.9 Notified Body's name and the Notified Body's single identification number

DQS Medizinprodukte GmbH
August-Schanz-Straße 21
60433 Frankfurt am Main
Germany
Tel.: +49 69 95427 300
Fax: +49 69 95427 388

E-Mail: medizinprodukte@dqs-med.de
Website: www.dqs-med.de
Single identification number: 0297

2 Intended use of the device

2.1 Intended purpose

The Neurovascular Flow Diverters are self-expanding, tubular vascular implants and allow the controlled and selective modulation of blood flow in extra- and intracranial arteries. In addition, the physical properties of the Neurovascular Flow Diverters straighten the target vessel slightly and reinforce it. These properties aid the endovascular reconstruction of diseased arteries along their cervical and intracranial course.

2.2 Indication(s) and target population(s)

The Neurovascular Flow Diverters are used for the treatment of vascular diseases:

- saccular and fusiform aneurysms and pseudoaneurysms,
- vascular dissections in the acute and chronic phases and
- vascular perforations and AV fistulae.

2.3 Contraindication(s) and/or limitations

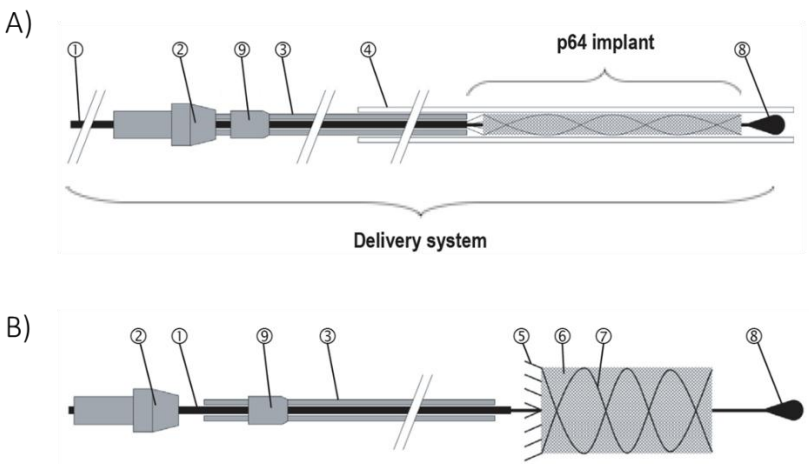
- Patients with an inadequate antiplatelet therapy or insufficient anticoagulant treatment according to standard medical practice before, during, and after the treatment.
- Angiography demonstrates the anatomic conditions are not appropriate for endovascular treatment.

3 Device description

3.1 Description of the device

The detailed structure of p64, p48 MW (HPC), p64 MW (HPC) and p48 LITE (HPC) is presented below.

The **p64** (Figure 1) is a tubular vascular implant and consists of 64 interwoven Nitinol wires. Two wires, which are located opposite one another, are wrapped by platinum spirals and ensure visibility under X-ray fluoroscopy. In addition, a platinum marker is located on each of the eight ends on the proximal end of the implant.

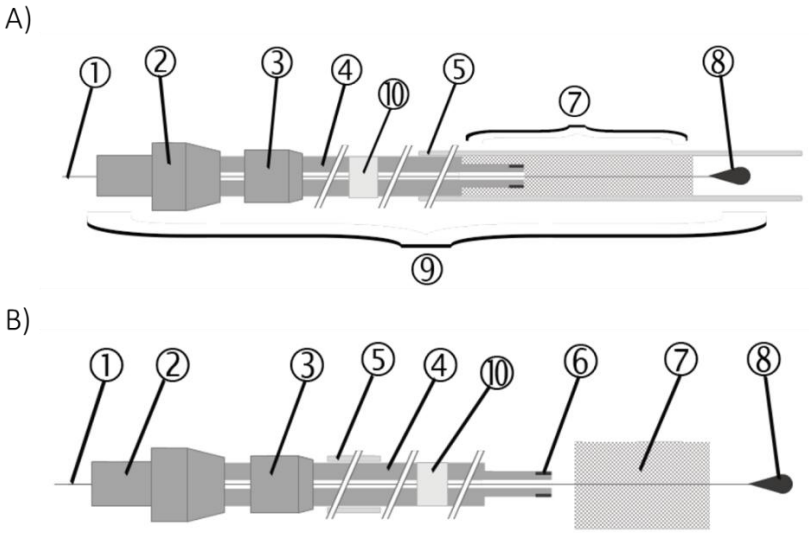


Legend:

1) Delivery wire
2) Torquer
3) Polymer tube (detachment tube)
4) Peel-away-sheath
5) Platinum marker
6) 64 interwoven nitinol wires/ Implant
7) Platinum spirals
8) Distal wire tip
9) Handle

Figure 1: A) p64 and delivery system **B)** Detached delivery system and deployed p64 implant.

The **p48 MW (HPC)/p64 MW (HPC)** (Figure 2) are tubular vascular implants that consist of 48/64 interwoven nitinol wires which are filled with a platinum core to ensure visibility under X-ray fluoroscopy.

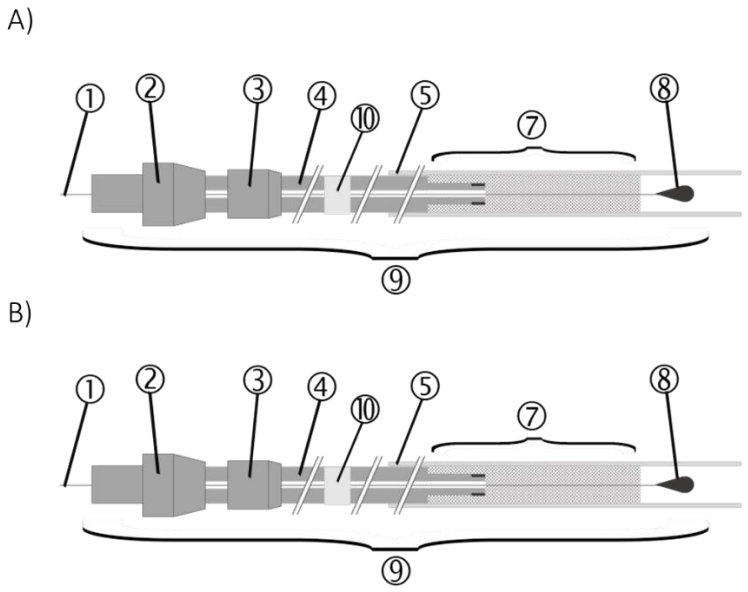


Legend:

1) Delivery wire
2) Torquer
3) Handle
4) Transport tube
5) Introducer sheath
6) Platinum marker
7) Implant
8) Distal wire tip
9) Delivery system
10) Fluorosafe Marker

Figure 2: A) p48 MW (HPC)/p64 MW (HPC) and delivery system in introducer sheath, B) Delivery system and detached p48 MW (HPC) implant.

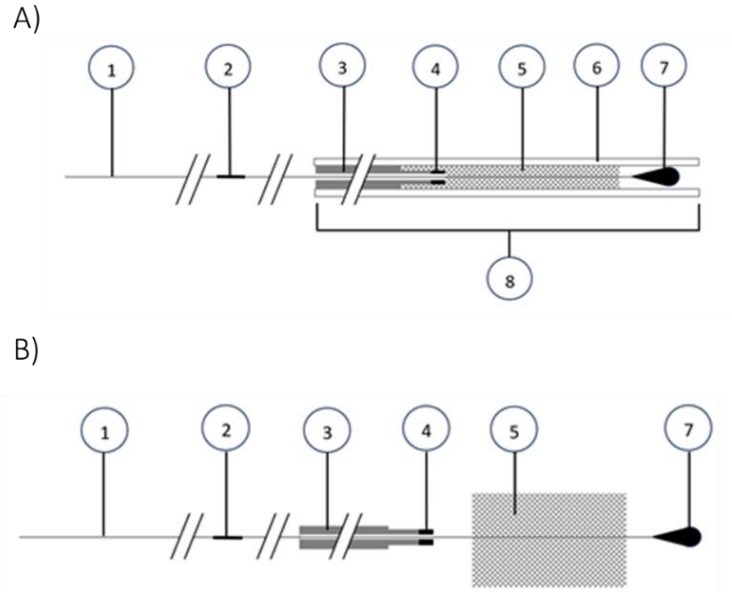
The **p48 MW (HPC)/p64 MW (HPC) Flow Modulation Devices with harmonized delivery system** (Figure 3) are tubular vascular implants that consist of 48/64 interwoven nitinol wires which are filled with a platinum core to ensure visibility under X-ray fluoroscopy. For the harmonized versions the same delivery system is used for both, the p48 MW (HPC) and the p64 MW (HPC).



Legend:

1) Core wire
2) Torquer
3) Handle
4) Transport tube
5) Introducer sheath
6) Platinum marker
7) Implant
8) Delivery wire
9) Delivery system
10) Fluorosafe Marker

Figure 3: A) p48 MW (HPC)/p64 MW (HPC) implants (harmonized delivery system) in introducer sheath added to the delivery system **B)** Delivery system, retracted introducer sheath and detached p48 MW (HPC)/p64 MW (HPC) implant.



Legend:

1) Delivery wire
2) Fluorosafe marker
3) Transport tube
4) Platinum marker
5) 48 interwoven nitinol wires/Implant
6) Introducer sheath
7) Distal wire tip
8) Delivery system

Figure 4: A) p64 MW (HPC) and delivery system in introducer sheath, **B)** delivery system and detached p64 MW (HPC) implant.

The **p48 LITE (HPC)** (Figure 4) is a tubular vascular implant and consists of 48 interwoven nitinol wires, each filled with a platinum core for visibility under X-ray fluoroscopy.

The **p48 MW HPC, the p64 MW HPC** and **p48 LITE HPC** are entirely covered with a hydrophilic polymer coating (HPC) which initially reduces the adhesion of platelets thrombocytes and thus reduces the risk of thrombus formation on the device surface (based on *in vitro* data [1-4]).

Materials

The implants consist of the biocompatible metals nitinol and platinum, the insertion system of various biocompatible metals (stainless steel or Cobalt-Chrome (CoCr) alloy, nitinol and platinum-iridium) as well as

various, also biocompatible plastics (mainly polyimide and Polytetrafluoroethylene (PTFE)). All materials that come in contact with the patient are listed in Table 2.

Table 2: Materials to come in contact with patient.

Device variant	Implant (long term contact)	Delivery system (short term contact)
p64	Nitinol, Platinum Iridium alloy	Nitinol, Stainless steel, Platinum Iridium alloy, Polyimide, Polytetrafluoroethylene (PTFE), Ethyl cyanoacrylate
p48 MW (HPC)	Nitinol, Platinum, **If applicable:** HPC (hydrophilic polymer coating) → Polysaccharides	Nitinol, Polyurethane, Polyimide, Platinum Iridium alloy, Polytetrafluoroethylene (PTFE), Ethyl cyanoacrylate, Thermoplastic polyurethane
p64 MW (HPC)		
p48 LITE (HPC)		Nitinol, Platinum Iridium alloy, Cobalt-Chrome Alloy, Polyurethane, Polyimide, Ethyl Cyanoacrylate
p48 MW (HPC) *harmonized system*		Nitinol, Polyurethane, Polyimide, Platinum Iridium alloy, Polytetrafluoroethylene (PTFE), Ethyl Cyanoacrylate, Tampapur TPU 970 White
p64 MW (HPC) *harmonized system*		

3.2 A reference to previous generation(s) or variants if such exist, and a description of the differences

The medical device group Neurovascular Flow Diverter, previously consisting of the product variants p64, p48 MW (HPC) and p64 MW (HPC), is CE-certified according to MDR and combines all MDD-certified flow diverter product families by phenox GmbH (p64, p48 MW (HPC) and p64 MW (HPC)) (see chapter 1.7).

Additionally, new product variants, i.e., p48 LITE (HPC), p48/64 MW (HPC) with harmonized delivery systems, are being introduced.

3.3 Description of any accessories which are intended to be used in combination with the device

The products have no accessories.

3.4 Description of any other devices and products which are intended to be used in combination with the device

The products of the medical device group Neurovascular Flow Diverter are compatible with equipment commonly used in interventional neuroradiology. This includes an angiography system, as well as sheaths, guide wires, microcatheters and other products for minimally invasive implantation of the devices. All p64 models are compatible with microcatheters which have an internal diameter of 0.027 inches. p48 MW (HPC) and p64 MW (HPC) with or without harmonized delivery system are compatible with microcatheters with an inner diameter of 0.021 inches. The p48 LITE (HPC) is compatible with microcatheters with an inner diameter of 0.017 inches.

4 Risks and warnings

In addition to the contraindications described in chapter 2.3, residual risks, warnings, adverse effects as well as possible complications and the associated harm has to be taken into account.

4.1 Residual risks and undesirable effects

The general terms risk and harm, residual risks and undesirable effects are defined as follows:

- ***Risk*** means the "combination of the probability of occurrence of harm and the severity of that harm".
- ***Harm*** is the "injury or damage to the health of people or damage to property or the environment".
- ***Residual risks*** are defined as a "risk remaining after risk control measures have been taken".
- ***Undesirable effects*** "can be understood as any undesirable side-effect related to the device and that is experienced by the patient and/or can be diagnosed and/or measured in the patient".

Residual risks and undesirable effects related to the use of Neurovascular Flow Diverter or the procedure, and their probability of occurrence are listed in Table 3. Both procedure-related and product-related risks are considered.

The undesirable effects and residual risks were identified in the literature on Neurovascular Flow Diverters (page 50) and are well known and adequately addressed in the risk management. Only publications in which an appropriate number of patients were treated were considered in order to avoid the percentage figures being biased by too small patient populations. In this case, the number was set at 50 patients. In some cases, it was not possible to comply with this figure because only articles with smaller populations were available. These figures are given in *italics*. In total, 34 publications were included in which only the p64, the p48 MW (HPC) and p64 MW (HPC) were used. Case reports were excluded.

Table 3: Undesirable effects and residual risks of Neurovascular Flow Diverter devices, the frequency of occurrence and their literature reference

Undesirable effects/Residual risk	Min. – Max. reported number [Reference]
Air Embolism	Not reported
Embolism in distal vessels	1/121 (0.8%) [5] - Not reported
Thrombosis	4/617 (0.6%) [6] - 2/121 (1.7%) [5]
In-stent thrombosis	4/1781 (0.2%) [7] - 2/79 (2.5%) [8]
Thromboembolism	2/1781 (0.1%) [7] - 3/74 (4.1%) [9]
(Transient) stenosis of target vessel	Not reported
In-stent stenosis (ISS)	1/1781 (0.06%) [7] - 16/84 (19%) [10]
Intimal hyperplasia	*5/22 (22.7%)* [11] - 29/108 (26.9%) [12]
Vasospasm	*3/48 (6.3%)* [13] - 9/84 (10.7%) [14]
Vessel occlusion	1/530 (0.2%) [6] - 1/121 (0.8%) [5]
Occlusion of side branch/perforator	2/420 (0.5%) [15] - 4/54 (7.4%) [16]
Cerebral ischemia	1/1781 (0.06%) [7] -4/54 (7.4%) [16]
Transient ischemic attack (TIA)	2/121 (1.7%) [5] - 3/100 (3%) [10]
Perforation	4/1781 (0.2%) [7] - 1/54 (1.9%) [16]
Rupture	1/1781 (0.05%) [7] - 1/100 (1%) [10]
Dissection	1/420 (0.2%) [15] - 1/54 (1.9%) [16]
Delayed aneurysm rupture	1/617 (0.2%) [6] - 1/72 (1.4%) [17]
Formation of a pseudoaneurysm	Not reported
Other arterial lesions	Not reported
Hemorrhage	1/420 (0.2%) [15] - 2/54 (3.7%) [16]
Bleeding	1/22 (4.5%) [11] - Not reported
Hematoma	1/530 (0.2%) [6] - 1/72 (1.4%) [17]
Hydrocephalus	Not reported
Stroke (ischemic and hemorrhagic)	1.1% [18] - 24/372 (6.4%) [15]
Infarction	1/530 (0.2%) [6] - 7/100 (7%) [10]

Undesirable effects/Residual risk	Min. – Max. reported number [Reference]
Neurological deficits	6/617 (0.3%) [6] - 11/79 (13.9%) [8]
Adverse reaction to antiplatelet/anticoagulation agents, anesthesia, radiation exposure	3/617 (0.5%) [6] - Not reported
Access site complications, e.g., groin hematoma	6/617 (1%) [6] - Not reported
Allergic reaction, infection	2/617 (0.3%) [6] - Not reported
Foreign body reaction	1/102 (1%) [19] - Not reported
Inflammation	1/79 (1.3%) [8] - *1/48 (2.1%)* [13]
Pain	Not reported
Edema	1/102 (1%) [19] - Not reported
Encephalopathy	Not reported
Extravasation	Not reported
Mass effect	2/617 (0.3%) [6] -Not reported
Persistent vegetative state	Not reported
Death	2/530 (0.4%) [6] - 1/54 (1.9%) [16]
Other	Not reported
Friction	Not reported
Inadequate apposition	*1/32 (3.1%)* [20] - Not reported
Unintentional release at an unplanned localization	*1/25 (4%)* [21] - Not reported
Detachment or deployment problems	3/617 (0.5%) [6] - 10/132 (7.6%) [19]
Incomplete opening	3/617 (0.5%) [6] - 4/108 (3.7%) [12]
Collapse	1/79 (1.3%) [8] - *1/29 (3.5%)* [22]
Fracture of implant and/or delivery system before or during the intervention§	Not reported
Separation failure§	Not reported
Migration	1/100 (1%) [10] - 1/54 (1.9%) [16]
Implant-Coil combination issues§	Not reported
Implant-implant combination issues§	Not reported
Implant-microcatheter combination issues§	Not reported
Deformation	*1/48 (2.1%)* [13] - 3/100 (3%) [10]
Resheathing problems	*1/7 (14.3%)* [23] - Not reported
(Fore)shortening	2/89 (2.2%) [14] - 8/100 (8%) [10]

* Manually calculated

§ Reports on this complication are available in the MAUDE database of FDA, but it is not possible to quantify them through these reports.

4.2 Warnings and precautions

Please refer to the respective IFUs.

4.3 Other relevant aspects of safety, including a summary of any field safety corrective action (FSCA including FSN)

Until 30.09.2024, no field safety corrective action (FSCA) including field safety notice (FSN) had to be initiated. No serious incidents were reported.

5 Summary of clinical evaluation and post-market clinical follow-up (PMCF)

The following text summarizes the results of the Clinical Evaluation and results of the Post-Market Clinical Follow-Up (PMCF). The systematic literature search conducted in this process considers published data (e.g.,

publications) as well as other relevant data sources (e.g., studies) on the clinical safety and performance of the medical device group Neurovascular Flow Diverter. Both favourable and unfavourable data regarding conformity with the general safety and performance requirements (GSPRs) of p64, p48MW (HPC) and p48 MW (HPC) are objectively considered.

5.1 Summary of clinical data related to equivalent device

p48 LITE (HPC) is considered equivalent to the existing p48 MW (HPC). The product variants with the new harmonized delivery system are considered equivalent to the existing variants of p48 MW (HPC) and p64 MW (HPC), respectively. Any identified difference with regard to clinical, technical, and biological characteristics were analyzed and none of these differences were determined to significantly affect clinical safety or performance.

5.2 Summary of clinical data from conducted investigations of the device before the CE-marking

Prior to MDR-CE certification, no clinical study was conducted as sufficient clinical evidence was generated with the MDD-CE certified devices ("legacy devices"). Furthermore, equivalence between the newer device variants to the existing ones was demonstrated. Therefore, clinical data provided are applicable to all equivalent device configurations.

In the following, data from PMCF activities for legacy devices are summarized.

p64 Flow Modulation Device

After MDD CE-certification of p64 (15.10.2012), clinical data of 2,326 patients were documented which showed that p64 is safe and effective for its indications. After a mean of 3.8 months, a sufficient occlusion rate, defined as complete occlusion and residual neck, of approx. 75.7% could be achieved. After a mean of 11.6 months, data revealed a sufficient occlusion in 84.6% of aneurysms. The stroke rate was 0.6% and mortality occurred in 1.3% of patients.

Furthermore, the single-arm prospective, multicenter Post Market Clinical Follow-up (PMCF) study Diversion-p64 [24] was conducted by phenox GmbH according to the German medical devices law (“Medizinproduktegesetz”; MPG) §23b to assess safety and effectiveness of the p64 for the treatment of intracranial aneurysms (IA). The study is registered at ClinicalTrials.gov (NCT02600364).
This PMCF study reflects the real-world practice in the treatment of IAs, and represents the largest prospectively performed flow diverter (FD) studies with 420 patients who underwent treatment with the p64 (mean age 55 ±12.0 years, 86.2% female) at 26 centres across 10 countries. The primary effectiveness endpoint was the rate of complete aneurysm occlusion (Raymond-Roy Occlusion Classification 1) and the primary safety endpoints were incidence of major stroke (ischemic or hemorrhagic) or neurological death at 3 - 6 months related to the treatment of the target aneurysm. The majority of aneurysms were unruptured (93.3%), whereas 1.67% of the aneurysms were acutely ruptured.
Intra-procedural complications occurred: thromboembolisms (4%), vessel perforations (0.47%), aneurysm perforation (0.24%) were reported. Intra-operative side branch occlusion occurred (0.47%) and difficulty of device detachment was recorded (0.71%). After a mean of 145 ±43 days, 71.7% of the aneurysms showed complete IA occlusion and 4.5% had residual neck, leading to 76.2% of adequate occlusion. After a mean of 375 ±73 days, complete aneurysm occlusion and residual neck were seen in 83.7% and 2.3% of the patients,

respectively, leading to 86.0% of adequate occlusion. A major procedure-related stroke occurred in 1.9% of cases, all being thromboembolic in nature. The mortality rate was 0.97%. No further episodes of major stroke or death between the first and second follow-up were reported. The secondary endpoints revealed a minor stroke rate of 6.4%. In total, 95.8% of patients who suffered from minor strokes, were reported to have an mRS 0 and one patient an mRS 2.

In-stent stenosis of any degree was seen in 15.4% of cases, most of them being mild (<50%). After a mean of 375 ±73 days, in-stent stenosis of any degree was seen in 8.7% of patients. The majority of these cases (5.5%) showed mild stenosis with only a single case of severe stenosis (≥75%).

This study demonstrates the success of the treatment with the p64 Flow Modulation Device with regard to the primary safety endpoint. Treatment with p64 is associated with an acceptable rate of serious neurological events and a low risk of mortality. Also, the high rate of complete aneurysm occlusion outweighs the treatment risks.

p48 MW and p48 MW HPC Flow Modulation Device

In total, 390 cases were documented with p48 MW HPC after MDD CE-mark approval (30.11.2018). Sufficient occlusion was achieved in 64.9% after a mean of 4.3 months and 66.7% after a mean of 9.3 months. 3.3% of patients suffered a stroke. The mortality rate was 1.6%.

A total of 244 cases were documented with p48MW. In 81.8% of aneurysms, a sufficient occlusion was achieved after a mean of 3.7 months and in 66.7% of aneurysms after a mean of 14 months. The stroke and mortality rates were 0.8% and 0.4%, respectively.

p64 MW and p64 MW HPC Flow Modulation Device

With p64 MW HPC, 626 cases were documented after MDD CE-certification (22.12.2019). A sufficient occlusion rate of approx. 78.5% was observed after a mean of 4.4 months. After a mean of 7.1 months, the rate of sufficient occlusion was approx. 84.6%. A stroke was observed in 0.6% of patients and mortality occurred in 1.1%.

The clinical data of the legacy devices demonstrate that p64, p48 MW (HPC) and p64 MW (HPC) are effective and safe for their intended purpose when used as per the Instructions For Use (IFU).

5.3 Summary of clinical data from other sources

Clinical experience with p64, p48 MW (HPC) and p64 MW (HPC) was reported in several single center and multicenter series showing low morbidity and mortality rates. In Table 10 – Table 12 the publications are listed separately for each product variant. In the following, a summary of some of the most recent studies is given, demonstrating the safe and effective use of the Neurovascular Flow Diverters.

Vivanco-Suarez *et al.* [7] published a systematic review and meta-analysis on the safety and efficacy of p64, p48 MW (HPC) and p64 MW (HPC). Twenty studies with 1,781 patients and 1,957 aneurysms (ANs) were included. The p64, p64 MW HPC, p48 MW and p48 MW HPC were used in 12, 4, 3 and 1 studies, respectively. With p48 MW (HPC), 149 patients with 156 ANs were treated (p48 MW: 127 ANs, p48 MW HPC: 29ANs). In all but two studies, the patients were administered dual antiplatelet therapy (DAPT). The authors concluded that both devices have an acceptable efficacy and favourable safety profile. Patient and aneurysm characteristics as well as the study results are summarized in Table 4.

Table 4: Patient and aneurysm characteristics and study outcomes published by Suarez *et al.* [7]

Patient characteristics	
Female	78.7%
Age range	20-89 years
Aneurysm characteristics	
Previously treated	14.9%
Ruptured	7.2% (n= 141)
Non-saccular morphology (including fusiform, blister-like, dissecting, and segmental disease)	3.2%
Aneurysm size	0.8 – 50 mm
Neck size	1 – 20 mm
Anterior circulation	93.1%
Results	
Intraprocedural technical events	4% (n = 54)
Results for p64/p64 MW HPC	**Results for p48 MW/ p48 HPC**
Technical success rate: 99%	Technical success rate: 100%
Adjunctive coiling: 7%	Adjunctive coiling: 4%
Complete occlusion rate at final FU (range 3 - 14.5 months): - 77% (for p64 and p64 MW HPC) - 65%(for p64 MW HPC)	Complete occlusion rate at final FU (range 2 - 13.1 months): - 67% (for p48 MW and p48 MW HPC) - 71% (for p48 MW HPC)
Retreatment rate: 1%	Retreatment rate: 3%
Complication rate: 2% (p64 MW HPC: 4%)	Complication rate: 3% (p48 MW HPC: 2%)
Overall mortality rate: 0.49%	Overall mortality rate: 2%

Bilgin *et al.* [25] published a meta-analysis comparing HPC coated and non-coated devices. Seventeen studies with 1,238 patients were included. The overall complete occlusion rate was 73.4% (95% CI 65.43% to 82.43%). No significant difference in complete occlusion rates was observed between the HPC coated (80%) and non-coated devices (71.3%) . The overall complete/near complete occlusion rate was 84.6% (95% CI 78.64% to 91.20%). Subgroup analysis did not show any significant difference between the different device variants (HPC coated: 84.8%; non-coated: 84.6%).

Ischemic complications were encountered in overall 5.8% (95% CI 4.56% to 7.35%) of cases. No significant difference was found between the subgroups (HPC coated: 7.3%; non-coated: 5.3%). For patients treated with HPC coated devices, administration of SAPT (5.5%; 95% CI 2.83% to 10.85%) and DAPT (7.1%; 95% CI 1.23% to 41.45%) resulted in comparable ischemic complication rates (p=0.79). The overall hemorrhagic complication rate was 2.2% (95% CI 1.56% to 3.29%). The subgroup analysis showed no significant differences between the HPC coated (3%;95% CI 1.48% to 6.32%) and non-coated devices (2%; 95% CI 1.32% to 3.15%). For patients who underwent treatment with HPC coated devices, the rates of hemorrhagic complications were comparable between the SAPT group (1.7%; 95% CI 0.52% to 6.09%) and the DAPT group (4.8%; 95% CI 1.46% to 16.24%) (p=0.25). The authors conclude that HPC coated devices are equally safe and effective as the non-coated devices. Furthermore, they state that Prasugrel monotherapy could effectively prevent ischemic complications in patients treated with HPC devices.

Hellstern *et al.* *[19]* examined prasugrel as SAPT in a patient population of 102 patients who were treated for 132 unruptured aneurysms with p64 MW HPC. All patients received a loading dose of 30 mg prasugrel as SAPT at least for three days prior to the procedure followed by doses of 10 mg per day. Effective anti-platelet responses were determined with a Multiplate Analyzer or VerifyNow test. After six months, the patient was switched to 100 mg ASA PO daily with an overlap of three days. The response tests were repeated approximately two weeks after the procedure. Intraprocedural and post-procedural complications were

encountered in 13.6% (18/132) of aneurysms and postprocedural or delayed complications in 8.8% (9/102) of patients. No intra- or peri-procedural thromboembolic complications were encountered under SAPT. Two patients developed an in-stent-thrombosis due to SAPT non-adherence (24h-30d). Complete recanalization could be achieved with mechanical thrombectomy and eptifibatide. In-stent stenoses (ISS) were detected in 2/132 aneurysms (1.5%) at 1-69 d FU of which one was mild and one was moderate. At the 70-180d FU, 18/95 aneurysms were found to have an ISS. Mild ISS cases were observed in 13, moderate in 1 and severe in 4 cases. Complete occlusion was achieved in 67.4% (64/95) of patients at first FU (70-180 days) and neck remnants were observed in 5.3% (5/95). Angiography at the second FU (181-500 days) revealed a complete occlusion in 78.4% (58/74) and near complete occlusion in 5.4% (4/74) of aneurysms. The authors concluded that the use of p64MW HPC with prasugrel SAPT is both safe and effective for saccular aneurysms of the anterior circulation.

Castro-Afonso *et al.* [26] reported two-years FU results of 21 patients treated with p48 MW HPC under Prasugrel only. The patients were administered prasugrel for 6 months followed by acetylsalicylic acid(ASA)until 24 months. No patient had neurologic deficits in the time from treatment to the 24 month follow-up. In-stent stenosis <25% and in-stent stenosis >75% were observed in 1/24 patient (4.1%) each. Complete aneurysm occlusion was achieved in 74% (20/27) of aneurysms at the 24 month FU. Four aneurysms (14.8%) had dome reduction, and three aneurysms (11.1%) remained unchanged.

In addition to clinical data, *in-vitro* [1-4] and *in-vivo* [27] studies show that the HPC coating (HPC: Hydrophilic Polymer Coating) of p48 MW HPC and of p64 MW HPC reduces the risk of thrombus formation on the device by initially reducing or preventing the adhesion of platelets to external surfaces being in contact with blood. Platelet aggregation inhibition must be confirmed by adequate tests (e.g., VerifyNow, PFA).

Ernst *et al.* [10] published their experiences on the safety and effectiveness of p64 MW HPC in treatment of unruptured aneurysms of both anterior and posterior circulation. In total, 100 patients were treated and all were administered dual antiplatelet therapy prior to treatment (Clopidogrel + ASA: 68; Ticagrelor + ASA: 24). The flow diverters opened instantaneously in 94 (94%) cases and good wall apposition was achieved in 96 (96%) cases. In three cases, a torsion of the FD with incomplete braid opening occurred. In another three cases, full device opening was achieved with a balloon or a stent-retriever. Device shortening was reported in 8 cases.

Overall, clinical peri- and post-procedural adverse events occurred in 16 cases (16%). One patient died three days after the treatment, probably due to pusherwire perforation resulting in a severe intracranial hemorrhage. Overall complete aneurysm occlusion was achieved in 61 of 84 (73%) followed cases, adequate occlusion (OKM C+D) was achieved in 78 of 84 (93%) of followed cases. Follow-up DSA was performed in 65 cases at mean 7± 3 months (range 1–22 months) and showed that most aneurysms (n=46) were completely occluded (OKM D). Three aneurysms underwent no change (OKM A) while one aneurysm exhibited subtotal filling (OKM B). In 15 cases neck remnants (OKM C) were detected. In-stent stenosis of any grade was found at follow-up in 19% of cases (n=16/84). Of these, high-grade stenosis (>75%) occurred in only one patient. Retreatment was necessary in one case due to device migration.

Publicly available information, i.e., other manufacturer's Summary of Safety and Clinical Performance (SSCP) Reports were searched for in the Eudamed database[a], but did not result in any hits in the reporting period.
In the reporting period, no public registry data were reviewed as none have been explicitly identified via the literature search. So far, no public registries with the focus on the indications of the products of the medical device group Neurovascular Flow Diverter are known. However, federal safety databases are regularly searched (e.g., FDA's MAUDE database) for incidents to determine whether there are new or unknown risks for competitor devices. In this way, it can be checked whether there are any new or unknown risks for the products of the medical device group Neurovascular Flow Diverter.

All phenox known clinical data, as well as published and unpublished data, have been made available for the compilation of the data to be considered in this SSCP. Data sources, other than the ones named above, were not taken into account.

5.4 An overall summary of the clinical performance and safety

The p64, p48 MW (HPC) and p64 MW (HPC) aid the endovascular reconstruction of diseased arteries through the selective modulation of blood flow, which may lead to a reduction in the risk of hemorrhagic stroke.
In conclusion, the results of sufficient occlusion rates achieved with Neurovascular Flow Diverters are in line with the data published in literature. In the largest flow diverter study so far, Bonafé *et al.*[24] documented an adequate occlusion rate of 76.2% after an average of 4.7 months in the Diversion-p64 study. At 1-year, the aneurysms further occluded achieving an adequate occlusion rate of 86.0%. Similar results were reported for similar devices by Shehata *et al.* [28]. Complete occlusion rate of 77% and 84.5% were achieved at the 1-year and 2-year FU, respectively. Based on these occlusion rates, it can be concluded that the devices are effective for their indication.
Clinical morbidity and mortality rates are within acceptable limits for all patients treated with any of the Neurovascular Flow Diverter devices. Own clinical data revealed a stroke between 0% and 3.3% and mortality rates between 0% and 1.5%. The Diversion-p64 study results, published by Bonafé *et al.*[24], report a permanent morbidity and mortality of 2.4%. Yarahmadi *et al.* [29] performed a meta-analysis with similar flow diverters and reported permanent morbidity in 3.3% and mortality in 1.7% of patients.
The HPC coating reduces the risk of thrombus formation by initially reducing or preventing the adhesion of platelets to external surfaces in contact with blood. This was demonstrated in *in vitro* studies [1-4], in an *in vivo* study [27]. As a consequence, implantation of p48 MW HPC and p64 MW HPC may be performed under the influence of only one antiplatelet inhibitor (SAPT) [7, 19, 25, 26, 30, 31]. The effectiveness of platelet aggregation inhibition has to be confirmed by suitable tests (e.g., Multiplate, VerifyNow).
The risks associated with Neurovascular Flow Diverter implantation are listed in Table 3 as also documented in the IFUs of the respective products. One of the most common complications was due to intimal hyperplasia (IH) which is a vascular reaction after flow diverter implantation and is very well known and can lead to stenosis. However, the rates vary a lot. For example, Luecking *et al.* [32] reported IH in 2.6% (2/78)

[a] https://ec.europa.eu/tools/eudamed - Eudamed will provide a living picture of the lifecycle of medical devices that are made available in the European Union (EU). Eudamed aims to enhance overall transparency, including through better access to information for the public and healthcare professionals, and to enhance coordination between the different Member States in the EU.

patients that were treated with FRED which led to in-stent stenosis. Kühn *et al.* [33] reported 35 cases (13.5%) of IH, of which 27 cases were mild, 5 cases were moderate and 3 were severe. Furthermore, IH was reported by Bhogal *et al.* [34] in 30% (9/30) patients at initial FU (mean 3.1 months). In all cases, the IH was asymptomatic. Eight of these patients had <50% and 1 patient 50-75%. In 6 patients the intimal hyperplasia resolved or improved and in 2 patients it remained stable (<50%). The number of vasospasms is also widely distributed. In the literature, a range between 4.5% [35] and 46.7% [36] was found. A further very common complication is in-stent stenosis (ISS). However, this includes both symptomatic and asymptomatic ISS of any degree without classification of the ISS severity which explains the high number.

A mortality rate between 0.4% - 1.9% was found in the literature on p64, p48 MW (HPC) and p64 MW (HPC) (see Table 3).

A critical assessment of the intended benefits of a treatment with these devices compared to the risks described in chapter 4, leads to the conclusion that the benefits clearly outweigh the identifiable risks. Based on this benefit-risk assessment, own clinical experience reported in chapter 5 and equivalence to own products, it can be concluded that the Neurovascular Flow Diverters are safe and effective.

5.5 Ongoing or planned post-market clinical follow-up (PMCF)

As part of the Post-Market Clinical Follow-Up (PMCF), clinical data are proactively and systematically collected and analysed on the basis of the indications, contraindications and intended purpose of the devices. This includes e.g., market feedback (e.g., customer complaints), literature analysis of phenox´s own products as well as literature and clinical data analysis regarding similar devices and analysis of federal safety databases (e.g., BfArM, FDA).

Further to the methods and procedures named above, several phenox initiated clinical studies are being performed. The COATING study (NCT04870047), is a prospective, multicenter randomized controlled trial with the aim to assess the safety and efficacy of the coated p64 MW HPC under SAPT and of uncoated p64 MW under DAPT. The study was set-up in compliance with the most current revision of ISO 14155 and in line with §74 of the Medical Device Regulation (MDR).

In addition, the investigator initiated trial (IIT) prospective, single-centre, single-arm randomized study DART is being conducted in Brazil to evaluate the safety and efficacy of the p48 MW HPC under SAPT and DAPT. First results were published by de Castro-Afonso *et al.* in 2021 [30] [37]. Two-year follow-up data has also been published [26].

6 Possible diagnostic or therapeutic alternatives

The ultimate goal of the treatment of intracranial aneurysms is complete and permanent occlusion of the aneurysm sac in order to completely obliterate the risk of rupture. A ruptured cerebral aneurysm is the most common cause of subarachnoid hemorrhage (SAH) which can lead to a hemorrhagic stroke and even to death.

Treatment options for unruptured intracranial aneurysms include preventive repair in the form of surgical (clipping) and endovascular methods (coiling and stenting). However, most aneurysms remain stable and the benefit of treating intracranial aneurysms must be carefully weighed against the potential risk of treatment [38]. Several factors must be taken into account for the management of ruptured aneurysms, namely the person’s clinical condition, the characteristics of the aneurysm, and the amount and location of the subarachnoid blood [39]. The National Institute for Health and Care Excellence (NICE) recommends

endovascular coiling or surgical clipping when interventional treatment is an option, or no interventional procedure combined with monitoring to verify clinical improvement and potentially reassess treatment options.

Medical treatment is only possible for low risk unruptured aneurysms and includes blood pressure control, moreover smoking cessation is recommended. It is recommended that untreated aneurysms are followed up regularly with periodic angiographic imaging.

Surgical treatment of aneurysms consists of exposure of the lesion through craniotomy and subsequent clipping of the abnormal vascular wall to stop the blood flow into the aneurysm [40]. Some aneurysms would per se be suitable for clipping, but the clinical circumstances such as advanced age or dependence on continuous anticoagulation or anti-aggregation increase the surgical risks. For these patients, a hemodynamic aneurysm treatment can be a viable option [41] [42].

Aneurysm management can also be done via a bypass by performing the excisions of the lesion and recanalization of the inflow and outflow arteries, with or without grafting [40]. This technique is not always recommended due to the mismatch diameter of arteries.

Endovascular coiling is a viable treatment option for intracranial aneurysms, although retreatment of aneurysms due to coil compaction or aneurysm recurrence occurs in up to 12% of the patients [43]. The risk of retreatment increases with unfavourable anatomy of the aneurysm, in particular the size of the neck width. Wide-neck aneurysms increase the risk of neurological deficit during treatment and are particularly difficult to treat with endovascular coiling because of the increased risk of coil protrusion into the parent artery.

In balloon-assisted coiling a balloon is used to create a temporary support for the coil. Balloon-assisted coiling is considered to be a safe alternative treatment method to simple coiling for aneurysms with a large neck [43].

Neurovascular stents are used as ancillary tools in stent-assisted coiling (SAC) of intracranial aneurysms. In stent-assisted coiling, a stent is placed to cover the neck of the aneurysm to provide a scaffold to protect the parent vessel and to allow coiling of complex aneurysms, such as wide-necked and fusiform aneurysms [43]. SAC is considered a safe alternative treatment method to surgical clipping of unruptured aneurysms [44]. Simple coiling and stent-assisted coiling have similar outcome and complication rates. The risk of aneurysm recurrence is lower after stent-assisted coiling, but there is an increased risk of thrombosis associated with the stent placement [45].

Dissections can be treated through various approaches depending on the severity and location of the dissection. The treatment options include medical management, surgical therapy involving surgical bypass and clipping as well as endovascular therapy using minimally invasive techniques such as (stent-assisted) coiling or stent placement and flow diverter stents [46].

In the case of recurring dissections despite medical treatment, endovascular treatment is considered a viable additional treatment alongside the anticoagulant medication. The Guidelines for Secondary Stroke Prevention recommend endovascular treatment in cases with definite recurring cerebral ischemic events [47]. There are examples of successful stent reconstruction of carotid dissections with acceptable immediate and long-term outcomes but further evaluation is needed [48].

The treatment for perforations involves directly sealing the perforation site with coils, liquid adhesives, a combination of both or balloon inflation. In the latter, a balloon is temporarily placed over the perforation site for several minutes, then deflated, and removed when no further extravasation is observed. [49]

The AWMF guideline [50] recommends various treatment methods for AVMs, including neurointerventional, neurosurgical and radiotherapeutic therapy. A distinction can be made between prophylactic therapy to eliminate a dangerous fistula and symptom-controlling (palliative) therapy. Endovascular treatment options include transarterial embolization with Onyx® and transvenous embolization using coils, which are well-established and have low complication rates. Particle or tissue adhesive embolization is less controllable and rarely leads to permanent closure of the fistula, so it should not be routinely used. Coils are commonly used for transvenous embolization, and in some cases, liquid embolization can be introduced through venous probing of the fistula, possibly combined with coil treatment. Neurosurgical treatment involves identifying the exact location of the fistula point and eliminating it through coagulation, transection, or clipping. Stereotactic radiotherapy is another option, although it is rarely used and suitable for specific cases with circumscribed fistulas or high-risk patients.

7 Suggested profile and training for users

The Neurovascular Flow Diverters may only be used in a (neuro-) radiological clinic by specialized, appropriately trained physicians who are experienced in the use of flow modulation devices. Participation in a product training course from phenox GmbH is recommended for the use of the product.

8 Reference to any harmonized standards and common specifications (CS) applied

The standards defined as the most important applicable standards are listed below:

- EN ISO 14630 *Non-active surgical implants - General requirements* (Status: 2009/2012)
- EN ISO 25539-2 *Cardiovascular implants - Endovascular implants - Part 2* (Status: 2020)
- ISO 17327-1 *Non-active surgical implants - Implant coating - Part 1* (Status: 2018)

Each individual requirement point of the respective standard is evaluated in the technical documentation. Applicable points are adopted as requirements in the technical documentation. If a point is not applicable, this is justified.

9 Revision history

Table 5: Revision history

SSCP Revision number	Date issued	Change description	Revision validated by the Notified Body
Rev. A	n/a, SSCP was updated before validation	Initial set-up of the document	☐ Yes Language of validation: English ☒ No

SSCP Revision number	Date issued	Change description	Revision validated by the Notified Body
Rev. B	Date of release by the Notified Body: 25.11.2023	Correction of the document title on the first page and in the footer (capital letters) and correction of the device storage requirements in chapter 4.2	☒ Yes Language of validation: English ☐No
Rev. C	n/a, SSCP was updated before validation	Update of content, in-line with annually updated CER and PSUR (data collection period PSUR: 31.12.2023).	☐ Yes Language of validation: English ☒No
Rev. D	Date of validation by the Notified Body: 06.05.2025	Update due to expansion of medical device group Neurovascular Flow Diverter with p48 LITE (HPC) and p48 MW (HPC) and p64 MW (HPC) with harmonized delivery system. Update with the findings from the updated Clinical Evaluation.	☒ Yes Language of validation: English ☐No

Summary of Safety and Clinical Performance (SSCP)

for the class III medical device group

Neurovascular Flow Diverter

consisting of

p64,

p48 MW (HPC), p64 MW (HPC)

and p48 LITE (HPC) Flow Modulation Devices

Patients and lay persons

Summary of safety and clinical performance for patients and lay persons

A summary of the safety and clinical performance of the medical device group Neurovascular Flow Diverter consisting of p64, p48/p64 MW (HPC) and p48 LITE (HPC) intended for patients and lay persons, is given in this part.

Document number: SSCP-FLOW DIVERTER
Document revision: Rev. D
Date of issue: Release date according to the Notified Body 06.05.2025

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the medical device group Neurovascular Flow Diverter. The information presented below is intended for patients or lay persons. A more extensive summary of its safety and clinical performance prepared for healthcare professionals is found in the first part of this document.

The SSCP is not intended to give general advice on the treatment of a medical condition. Please contact your healthcare professional in case you have questions about your medical condition or about the use of the device in your situation. This SSCP is not intended to replace an implant card or the Instructions For Use (IFU) to provide information on the safe use of the device.

Terms, abbreviations and definitions

Term	Definition
Adequate occlusion	Complete exclusion or near complete exclusion of the aneurysm from the blood circulation.
Aneurysm	Bulge or weakening in the wall of a blood vessel.
Angiographic techniques	Imaging, radiological procedure in which the vessels are filled with contrast medium and made visible with the help of X-rays, magnetic resonance tomography or computer tomography.
Anticoagulation	Medical treatment used to prevent blood clots from forming or to break up existing blood clots in the body with the help of blood thinners.
Artery	Blood vessel that takes blood away from the heart to other parts of the body.
Balloon angioplasty	Medical procedure used to treat vessels that become narrow or blocked. During the procedure, a balloon is inflated temporarily in the target vessel to widen it and improve the blood flow.
Basic UDI-DI	*Basic Unique Device Identification - Device Identifier* Used to identify and register medical devices on the European Union market.
Cervical	Cervical refers to the area of the body related to the neck.
Clinical morbidity	The state of suffering from a disease or medical condition.
Coil	Thin wires mostly made of platinum which are designed to pack tightly into the aneurysm, promoting blood clotting and preventing aneurysm rupture.
Complete aneurysm occlusion	Complete exclusion of the aneurysm from the blood flow.
Contraindication	Reason against the treatment.
Craniotomy	Surgical operation in which a bone flap is temporarily removed from the skull to access the brain.

Term	Definition
DAPT	*Dual Antiplatelet Therapy* Usage of two platelet function inhibitors which are medications that reduce the ability of platelets, a type of blood cell involved in clotting which stick together and form blood clots.
Endovascular	Within the blood vessels
Dissection	A tear or rupture in the arterial wall leading to separation of the layers of the arterial wall; both acute and already known (chronic).
Femoral artery	Large artery located in the thigh region of the body. It is one of the major arteries supplying blood to the lower extremities.
FSCA	Feld Safety Corrective Actions
FSN	Field Safety Notices
Hemorrhage	Bleeding
Hemorrhagic stroke	Type of stroke that occurs when there is bleeding in the brain. It is usually caused by the rupture or leakage of a blood vessel in the brain.
HPC	*Hydrophilic Polymer Coating* Coating that imitates the natural lining of the inner vessel wall to prevent the platelets from recognizing the implant as a foreign body and thereby initially reduce the risk of thrombus (=blood clot) formation.
IFU	*Instructions For Use* Information provided by the manufacturer to inform about the intended purpose, correct use, and any precautions.
Imaging technique	Technique used to clearly visualize blood vessels e.g., Digital Subtraction Angiography – DSA.
Indication	Reason for treatment
Infarction	Condition in which an area of tissue or organ undergoes cell death due to a lack of blood supply.
Intended purpose	The use for which a device is intended.
Intracranial	Within the skull
Interventional neuroradiology	Medical subspecialty that uses minimally invasive techniques to diagnose and treat diseases of the brain, spine, and central nervous system.
Ischemic	Inadequate blood supply to a particular organ or tissue.
Ischemic stroke	Type of stroke that occurs when a blood vessel supplying oxygen and nutrients to the brain becomes blocked or narrowed, leading to decreased blood flow to a specific region of the brain.
Microcatheter	Thin flexible tube that is used in medical procedures to deliver medications, contrast agents, or other fluids and medical devices, such as neurovascular stents to specific locations in the body.
(Micro) Guidewire	(Micro) Guidewires are thin flexible wires which are used to navigate the microcatheter (= thin flexible tube) and thus the respective device to the target lesion.
MRA	*Mutual recognition agreements* MRAs are trade agreements that aim to facilitate market access and encourage greater international harmonization of compliance standards while protecting consumer safety.
MRI	*Magnetic Resonance Imaging* Non-invasive medical imaging test that produces detailed images of almost every internal structure in the human body, including blood vessels.
mRS score	*modified Rankin Scale* Score that is used to assess your/the patient's condition and indicates the degree of functional independence.
Neurological deficits	Abnormalities or impairments in the structure or function of the nervous system, which includes the brain, spinal cord, and nerves.

Term	Definition
NIHSS	*National Institutes of Health Stroke Scale* Scale that assesses stroke-related neurologic deficits
Platelet	Small, colorless blood cells, also known as thrombocytes, that are essential for blood clotting.
Platelet function inhibitor	Medication that reduces the ability of platelets, a type of blood cell involved in clotting which stick together and form blood clots.
PMCF	*Post-Market Clinical Follow-Up* Manufacturer collects and evaluates clinical data from the use of the approved device.
Pseudoaneurysm	A „false“ aneurysm which involves a dilatation of the arterial wall which is caused by a disruption in the arterial wall. Pseudoaneurysms occur because of trauma, such as a puncture or rupture of an artery during a medical procedure or an injury.
Rupture	Sudden breaking or bursting
SAH	*Subarachnoid hemorrhage* Bleeding in the space that surrounds the brain.
SAPT	*Single Antiplatelet Therapy* Usage of one platelet function inhibitor which is a medication that reduces the ability of platelets, a type of blood cell involved in clotting which stick together and form blood clots.
SSCP	*Summary of Safety and Clinical Performance* Provides public access to an updated summary of the main aspects of the safety and clinical performance of the medical device group.
Stenosis	Narrowing of an artery/vessel
Stroke	Medical condition that occurs when the blood supply to a part of the brain is interrupted or reduced, depriving the brain tissue of oxygen and nutrients. This can cause brain cells to die within minutes.
Thrombocyte	Small, colorless blood cell, also known as platelet that is essential for blood clotting.
Thrombogenicity	Ability of a substance or material to promote the formation of blood clots.
Thrombus	Blood clot
Thrombosis	Formation of a blood clot (thrombus) within a blood vessel, obstructing the flow of blood through that vessel.
Vasospasm	Sudden constriction- usually- of an arterial vessel.

1 Device identification and general information

Device trade name

The medical device group Neurovascular Flow Diverter consists of the p64, p48/p64 MW (HPC) and p48 LITE (HPC) (Table 6). The product family p48 MW (HPC) consists of p48 MW and p48 MW HPC. The device versions with the suffix HPC carry a hydrophilic polymer coating which is explained in chapter 3.
Please note that in the following the term p48 MW (HPC) refers to both device versions p48 MW (uncoated) and p48 MW HPC (coated). The same applies for p64 MW (HPC) and p48 LITE (HPC).

Table 6: Products of the medical device group Neurovascular Flow Diverter

Medical device group	Neurovascular Flow Diverter										
Basic UDI-DI	426012378FlowDiverterSV										
CE-certificate ID (Date of certification)	170781226 (21.12.2023)					1000236360 (28.08.2025)					
Product family	PAX-Flow Modulation Device										
Design variant	p64	p48 MW	p48 MW HPC	p64 MW	p64 MW HPC	p48 LITE	p48 LITE HPC	p48 MW*	p48 MW HPC*	p64 MW*	p64 MW HPC*
REF number: XX(X) – Model size	P64-XXX-XX	P48-MW-XXX-XX	P48-MW-HPC-XXX-XX	P64-MW-XXX-XX	P64-MW-HPC-XXX-XX	P48-LT-XXX-XX	P48-LT-HPC-XXX-XX	P48-MW-XXX- XX	P48-MW-HPC-XXX-XX	P64-MW-XXX -XX	P64-MW-HPC-XXX-XX

*harmonized delivery system

Manufacturer; name and address

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E-Mail: mailto:info@wallabyphenox.com
Website: www.phenox.net

Basic-UDI-DI (Device identification number)

The device identification number, also known as *Basic-UDI-DI* (Unique Device Identification - Device Identifier), is used to identify and register medical devices on the European Union market. The *Basic-UDI-DI* for the medical device group Neurovascular Flow Diverter is 426012378FlowDiverterSV.

Year when the device was first CE-marked

- p64 was certified for the first time on 15.10.2012 under the Medical Device Directive (MDD) (Certificate number: 506681 MRA).
- p48 MW (HPC) was certified for the first time on 30.05.2018 under the Medical Device Directive (MDD) (Certificate number: 539671 MRA).
- p64 MW (HPC) certified for the first time on 22.12.2018 under the Medical Device Directive (MDD) (Certificate number: 547128 MRA).
- The medical device group Neurovascular Flow Diverter got CE-certified under the Medical Device Regulation (MDR) on 21.12.2023 (Certificate ID: 170781226).
- p48 LITE (HPC), p48 MW (HPC), and p64 MW (HPC) with harmonized guidance system got CE-certified under MDR on 28.08.2025 (Certificate ID: 1000236360).
-

2 Intended use of the device

Intended purpose

The Neurovascular Flow Diverters are self-expanding, tubular vascular implants and allow the controlled and selective modulation of blood flow in extra- and intracranial (= *outside and inside of the brain*) arteries (=*blood vessel that takes blood away from the heart to other parts of the body*). In addition, the physical properties of the Neurovascular Flow Diverters straighten the target vessel slightly and reinforce it. These properties aid the endovascular reconstruction of diseased arteries along their cervical (= *area of the body related to the neck*) and intracranial course.

Indications and intended patient groups

The Neurovascular Flow Diverters are used in the endovascular treatment of vascular diseases:

- saccular and fusiform aneurysms and pseudoaneurysms,
- vascular dissections in the acute and chronic phases and
- vascular perforations and arteriovenous fistulae.

Further information about the above-mentioned vascular diseases can be found in Table 7.

Table 7: Type of diseases treated by Neurovascular Flow Diverter devices.

Type of disease	Explanation
Saccular (or berry-like) aneurysms	A balloon-shaped bulge in an artery which is caused by weakness in the vessel wall. An aneurysm is a dilatation or a bulge in a blood vessel which is caused by weakness in the vessel wall. The most common place for their occurrence is arteries, which are vessels that transport blood away from the heart to the rest of the body. In such arteries the blood pressure can cause small areas to bulge outwards like a balloon. These bulges carry a risk of rupture leading to bleeding into the space between the brain and the tissue covering the brain.

Type of disease	Explanation
	This condition is known as “subarachnoid hemorrhage” (SAH) and causes approximately 5% of all strokes worldwide [51, 52].
Fusiform (or helical-shaped) aneurysms	An irregularly dilated artery.
Pseudoaneurysm	A „false“ aneurysm which involves a dilatation of the arterial wall which is caused by a disruption in the arterial wall. Pseudoaneurysms occur because of trauma, such as a puncture or rupture of an artery during a medical procedure or an injury.
Dissections	A tear or rupture in the arterial wall leading to separation of the layers of the arterial wall; both acute and already known (chronic).
Vessel perforation	An injury to a vessel/a hole in a vessel or artery.
Arteriovenous fistulae	Abnormal connection between the oxygen-rich (arterial) and oxygen-poor (venous) blood vessel.

Contraindications and limitations

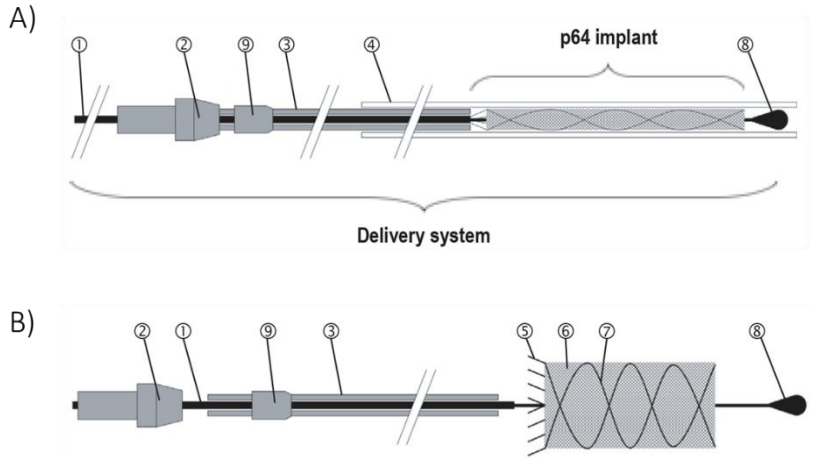
- Patients with an inadequate antiplatelet therapy or insufficient anticoagulant treatment according to standard medical practice before, during, and after the treatment.
- Angiography demonstrates the anatomic conditions are not appropriate for endovascular treatment.

3 Device description

Device description and material/substances in contact with patient tissues

In the following, a short summary of the design for each device is given.

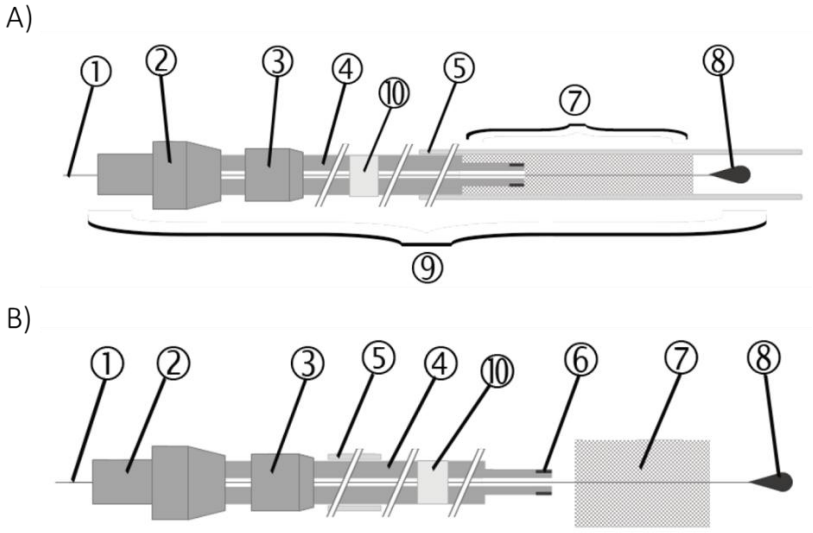
The **p64 Flow Modulation Device** is a tubular vascular implant and consists of 64 interwoven nitinol wires ⑥. Since nitinol is not sufficiently radiopaque *(= not allowing the passage of X-rays or other radiation*), 2 wires of the braid ⑦, which are in opposite positions, are wrapped by platinum spirals to ensure visibility under X-ray fluoroscopy. In addition, a platinum marker is located on each of the eight ends ⑤ on the proximal end of the implant.



Legend:
1) Delivery wire
2) Torquer
3) Polymer tube (detachment tube)
4) Peel-away-sheath
5) Platinum marker
6) 64 interwoven nitinol wires/ Implant
7) Platinum spirals
8) Distal wire tip
9) Handle

Figure 5: A) p64 Flow Modulation Device and delivery system, B) detached delivery system and deployed p64 implant.

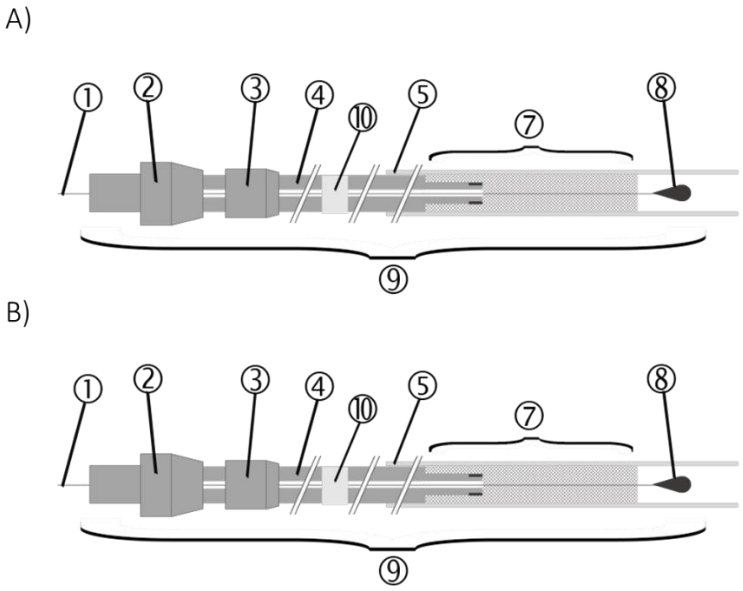
The **p48 MW (HPC)/ p64 MW (HPC) Flow Modulation Devices** are tubular vascular implants that consists of 48 and 64 interwoven nitinol wires, respectively ⑦ which are filled with a platinum core to ensure visibility under X-ray fluoroscopy.



Legend:
1) Delivery wire
2) Torquer
3) Handle
4) Transport tube
5) Introducer sheath
6) Platinum marker
7) Implant
8) Distal wire tip
9) Delivery system
10) Fluorosafe

Figure 6: A) p48 MW (HPC)/p64 MW (HPC) Flow Modulation Devices and delivery system in introducer sheath B) Delivery system and detached p48 MW (HPC)/p64 MW (HPC) implant.

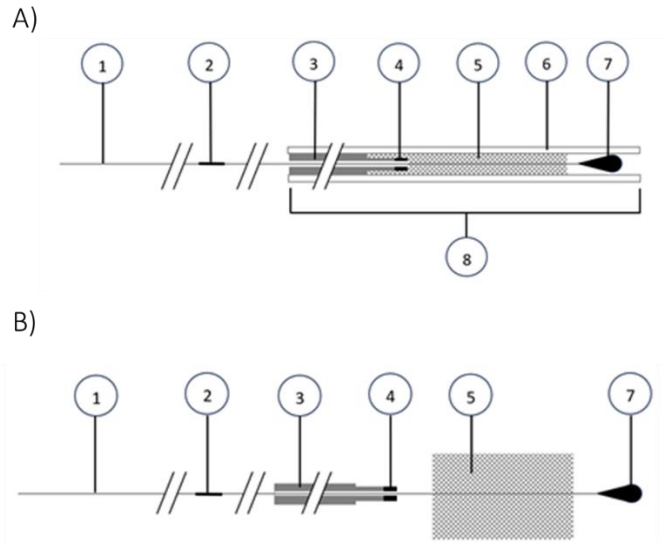
The **p48 MW (HPC)/p64 MW (HPC) Flow Modulation Devices with harmonized delivery system** are tubular vascular implants that consist of 48/64 interwoven nitinol wires which are filled with a platinum core to ensure visibility under X-ray fluoroscopy and have a harmonized delivery system.



Legend:
1) Core wire
2) Torquer
3) Handle
4) Transport tube
5) Introducer sheath
6) Platinum marker
7) Implant
8) Delivery wire
9) Delivery system
10) Fluorosafe Marker

Figure 7: A) p48 MW (HPC)/p64 MW (HPC) implants (harmonized delivery system) in introducer sheath added to the delivery system B) Delivery system, retracted introducer sheath and detached p48 MW (HPC)/p64 MW (HPC) implant.

The **p48 LITE (HPC) Flow Modulation Device** is a tubular vascular implant and consists of 48 interwoven nitinol wires, each filled with a platinum core for visibility under X-ray fluoroscopy. The term p48 LITE (HPC) indicates both device versions, p48 LITE (uncoated) and p48 LITE HPC (coated).



Legend:

1) Delivery wire
2) Fluorosafe marker
3) Transport tube
4) Platinum marker
5) 48 interwoven nitinol wires/Implant
6) Introducer sheath
7) Distal wire tip
8) Delivery system

Figure 8: A) p48 LITE (HPC) Flow Modulation Device and delivery system in introducer sheath B) Delivery system and detached p48 LITE (HPC) implant.

In case you have further questions regarding the devices, please contact your/the doctor.

The implants are in long term contact with the patient while the delivery system has only short-term contact. All materials that come in contact with the patient are listed in Table 8. To date, phenox has not received any reports regarding hypersensitivity to any of the materials listed in Table 8.

Table 8: Materials to come in contact with patient.

Device variant	Implant (long term contact)	Delivery system (short term contact)
p64	Nitinol, Platinum Iridium alloy	Nitinol, Stainless steel, Platinum Iridium alloy, Polyimide, Polytetrafluoroethylene (PTFE), Ethyl cyanoacrylate
p48 MW (HPC)	Nitinol, Platinum, **If applicable:** HPC (hydrophilic polymer coating) → Polysaccharides	Nitinol, Polyurethane, Polyimide, Platinum Iridium alloy, Polytetrafluoroethylene (PTFE), Ethyl cyanoacrylate, Thermoplastic polyurethane
p64 MW (HPC)		
p48 LITE (HPC)		Nitinol, Platinum Iridium alloy, Cobalt-Chrome Alloy, Polyurethane, Polyimide, Ethyl Cyanoacrylate
p48 MW (HPC) *harmonized system*		Nitinol, Polyurethane, Polyimide, Platinum Iridium alloy, Polytetrafluoroethylene (PTFE), Ethyl Cyanoacrylate, Tampapur TPU 970 White
p64 MW (HPC) *harmonized system*		

Information about medicinal substances in the device

Neurovascular Flow Diverters do not contain any medical substances.

Description of how the device is achieving its intended mode of action

Neurovascular Flow diverters have a very dense mesh and are used to treat, e.g., aneurysms. Their primary goal is to reconstruct the diseased vascular segment harboring the lesion. In addition, the physical properties

of the Neurovascular Flow Diverters straighten the target vessel slightly and reinforce it. These properties aid the reconstruction of diseased arteries.

During the procedure, a suitable microcatheter *(= thin flexible tube)* is used to deliver the flow diverter at the target position. The microcatheter is inserted into the femoral artery *(= large artery located in the thigh region of the body. It is one of the major arteries supplying blood to the lower extremities; refer to Figure 9)* and is advanced to the location of the brain aneurysm. Once in position, the flow diverter can be deployed and detached.

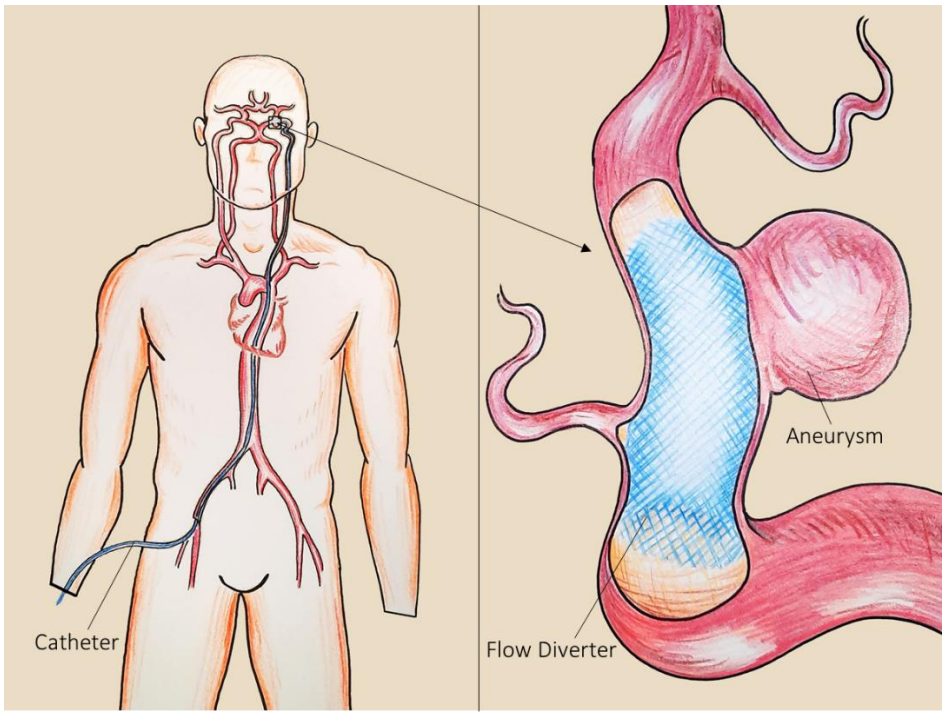


Figure 9: Route of the microcatheter into the aneurysm through the right femoral artery. Drawing by Mark Hobert (phenox) and inspired by Brisman *et al.* (2006)[53].

The influence of flow diversion on the aneurysm can be divided into three stages as depicted in Figure 10: hemodynamic (b), thrombus formation (c), and endothelialization (d).
Flow diverters are placed within the supplying artery (= *parent artery*) in which the aneurysm is located. They form a physical barrier at the interface between the aneurysm and the supplying vessel. The placement of this mesh structure leads to a reduction of blood flow into the aneurysm which reduces blood flow activity within the aneurysm and induces a stasis in the aneurysm in the first stage. In the second stage, the blood in the aneurysm begins to form a thrombus which can take up to several days or weeks. Flow diverters serve as a supportive scaffold in the last stage for the development of tissue across the aneurysm neck. At this point the fine-mesh structure is paved over by a new arterial wall lining. The thrombosed aneurysm is then reabsorbed by the body´s wound healing mechanism. The end result of this is a remodelled vessel returned to its normal physiological state.

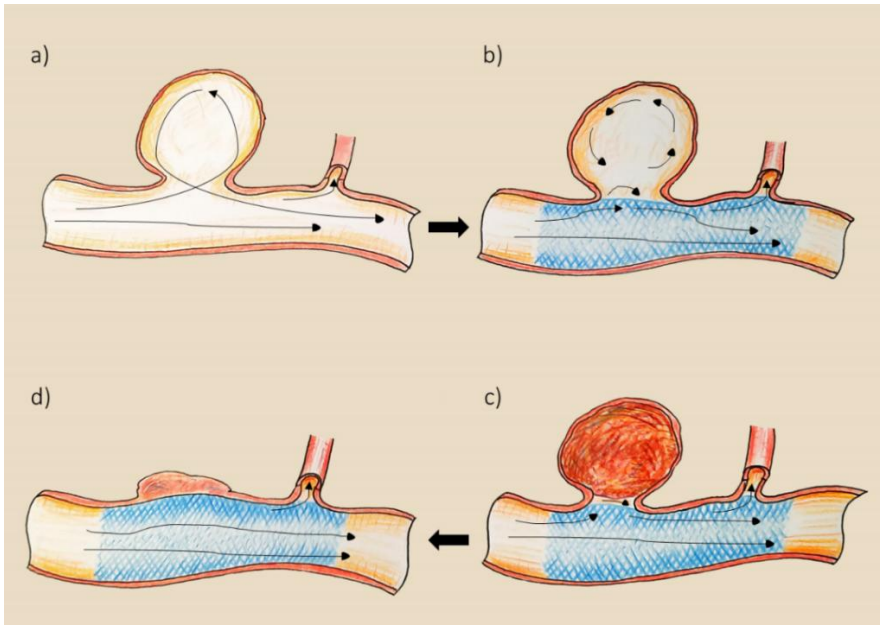


Figure 10: Simplified diagram of the mechanism of flow diverters: **a)** blood flow in an untreated aneurysm, **b)** reduced blood flow with implantation of flow diverter, **c)** clot formation within the aneurysm and stoppage of blood flow into the brain aneurysm, **d)** growth of tissue over flow diverter and aneurysm resorption. Drawing by Mark Hobert (phenox GmbH) and inspired by Dholakia *et al.* (2017)[54].

In case of dissections, the flow diverter is placed in the affected artery in order to seal the tear and redirect blood away from the dissection and thus promote healing. When a perforation occurs, the flow diverter can be deployed to redirect blood flow away from the site of the perforation, allowing the vessel to heal and preventing further complications such as hemorrhage. The flow diverter acts as a scaffold, supporting the damaged vessel and promoting the formation of new tissue to seal the perforation. During the treatment of arteriovenous fistula, the flow diverter is expanded to cover the abnormal connection. This helps to reduce the flow of blood through the fistula.

The HPC coating (Hydrophilic Polymer Coating) of p48 MW HPC, p64 MW HPC and p48 LITE (HPC) covers the entire implants. In Figure 11, the mechanism of the HPC coating is presented. HPC reduces the initial adherence of platelets and thus lowers the risk of blood clotting. This was demonstrated in *in vitro* studies [1-4], in an *in vivo* study [27].

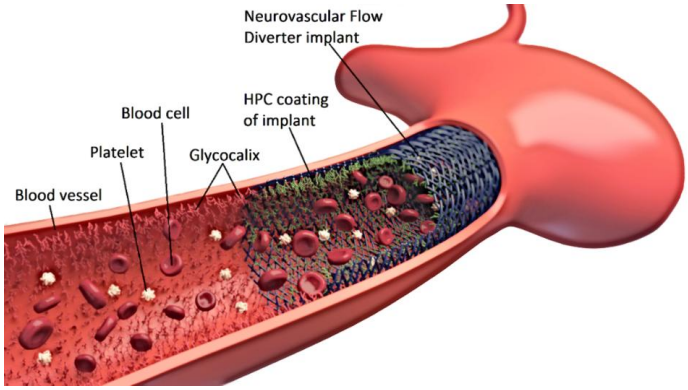


Figure 11: Operating principle of HPC (Hydrophilic Polymer Coating)

Description of accessories

The medical device group Neurovascular Flow Diverter has no accessories.

The devices are compatible with equipment commonly used in interventional neuroradiology *(= medical subspecialty that uses minimally invasive techniques to diagnose and treat diseases of the brain, spine, and central nervous system)*. This includes products for minimally invasive implantation of the device, such as microcatheters.

Every patient to be treated with a product from the medical device group Neurovascular Flow Diverter is supplied with an implant card. This is included in the product box, and is to be filled out by your/the treating doctor and handed over to you/the patient after the treatment. **You/The patient will be instructed to carry this implant card with him/her.** The implant card includes a scannable QR-Code, the patient's identifying information, as well as the direct website domain that contains the patient relevant information. In addition to the patient's first and last name, the implant card contains all important information about the implant itself, the manufacturer of the product, as well as the date of implantation and the responsible medical institution and healthcare professional.

4 Risks and warnings

Contact your healthcare professional if you believe that you are experiencing side-effects related to Neurovascular Flow Diverters or if you are concerned about risks. This document is not intended to replace a consultation with your healthcare professional if needed.

How potential risks have been controlled or managed

This part describes how risks will be reduced and also possible treatment options are described.
Before implantation of the flow diverter, the correct device size has to be selected by the doctor. Also, the selected flow diverter must be checked for damage before use. In general, implants are not allowed to be used if these are deformed or damaged, as function cannot be assumed otherwise.

Neurovascular Flow Diverters are in contact with blood, sodium chloride solution, X-ray contrast media, foreign products / materials (e.g., coils= *thin threads mostly made of platinum*), blood thinning agents. Neither of the Neurovascular Flow Diverters contain ingredients which, if used separately, may be considered as medical substances.
The implantation of flow diverters in general requires the administration of two platelet function inhibitors (= *medications which prevent blood clotting)*. Usually two platelet function inhibitors ("dual antiplatelet therapy" = DAPT) are given in appropriate doses. If justified by individual circumstances, the HPC devices may allow the implantation under single antiplatelet medication (SAPT). This was demonstrated in several publications [7, 19, 25, 26, 30, 31]. **If you have any questions regarding the agents, please consult your doctor.** The effectiveness of the given medication should be verified by an appropriate test (e.g., Multiplate or VerifyNow). Implantation of a product of the medical device group Neurovascular Flow Diverter in a patient without effective platelet function inhibition can lead to severe complications. **Please contact your/the doctor, if you have questions regarding this topic.**
Stroke (= *interruption of blood supply to the brain*) may occur as a result of flow diverter implantation. There are two types of strokes, ischemic (= *forming of clots*) stroke and hemorrhagic (= *bleeding*) stroke. Ischemic stroke is caused by a sudden reduction in blood flow to the brain, known as ischemia (= *cerebral ischemia*),

resulting in an inadequate supply of oxygen and glucose. The reduced blood flow is usually caused by narrowing (= *stenosis*) or occlusion (= *thrombosis*) of the arteries supplying the brain. The ischemia can be reversible or leads to the death of nerves and other brain cells. It is the doctor´s decision how to proceed and depends on different factors e.g., condition of the patient. Please contact your/the doctor, if you have questions regarding this topic.

Some of the important complications that can occur during or after a treatment are explained in the following section.

Stroke *(= medical condition that occurs when the blood supply to a part of the brain is interrupted or reduced, depriving the brain tissue of oxygen and nutrients)* may occur as a result of flow diverter implantation. There are two types of strokes, ischemic stroke and hemorrhagic stroke. Ischemic stroke is caused by a sudden reduction in blood flow to the brain, known as ischemia resulting in an inadequate supply of oxygen and glucose. The reduced blood flow is usually caused by a stenosis *(= narrowing)* or thrombosis *(= formation of a blood clot within a blood vessel)* of the arteries supplying the brain. Hemorrhagic stroke is the most feared complication. In this case, intracerebral hemorrhage *(= bleeding into the brain tissue)* or subarachnoid hemorrhage *(= bleeding between the inner and middle layers of the brain)* occur, e.g., due to a vessel rupture *(= sudden breaking or bursting*) or a vessel injury. Such bleedings can lead to a so-called vasospasm *(= sudden constriction - usually - of an arterial vessel).* As a result of the reduction in blood flow to the brain due to sudden constriction, the brain tissue is not receiving enough oxygen and can die, as in the case of an ischemic stroke. If a vasospasm occurs, it can be treated with medications that promote widening of the vessel, balloon angioplasty *(= widening of the affected artery with temporary inflation of a balloon)* aiming at widening the vessel, or a combination of these techniques. It is the doctor's decision how to proceed and depends on different factors e.g., condition of you/the patient. **Please contact your/the doctor, if you have questions regarding this topic.**

A so-called "false aneurysm" or "pseudoaneurysm" can occur after a dissection (= *splitting of the wall layers of an artery*) or after vessel injury. Pseudoaneurysms typically occur when there is an injury in the vessel wall so that blood leaks through the inner vessel wall but is retained by the outer vessel wall. Pseudoaneurysms can be treated by flow diverters.

After the implantation of a flow diverter, it may occur that side branches or adjacent vessels are covered by the flow diverter. In this case, it is the doctor's decision how to proceed and depends on different factors e.g., condition of your/the patient's health. For example, the flow diverter can be changed for a different size.

Please note that after flow diverter implantation you/the patient will have control visits. During these visits, your/the doctor will check your health condition and control the position of the flow diverter and the status of the aneurysm via imaging techniques (= *technique used to clearly visualize blood vessels, e.g., Digital Subtraction Angiography – DSA*). In some cases, an aneurysm has to be retreated for example because of aneurysm regrowth. In this case it is the doctor's decision how to proceed. For example, another flow diverter can be implanted. **Please contact your/the doctor, if you have questions regarding this topic.**

Remaining risks and undesirable effects

The following clinical terms are used in Table 9.

- **(Air) Embolism** = blockage of a blood vessel by air, foreign or body-own substances that have entered the bloodstream

- Dissection = tear or rupture in the inner lining of an artery, leading to the separation of the layers of the arterial wall
- Embolism / thromboembolism = a blockage-causing blood clot inside a blood vessel
- Encephalopathy = group of conditions that cause brain dysfunction
- Extravasation = leakage of a fluid out of its contained space into the surrounding area, e.g. contrast agent
- Hematoma = is a localized collection of blood outside of blood vessels, typically due to a rupture or injury to the blood vessels.
- Hemorrhage = bleeding, typically occurring from damaged blood vessels
- Hydrocephalus = condition in which an accumulation of brain fluid (= cerebrospinal fluid) occurs within the brain.
- Infarction = refers to the process of tissue death (necrosis) due to a lack of blood supply, typically caused by obstruction of blood flow. This obstruction can result from various factors, including thrombosis, embolism or vasospasm.
- Ischemia = inadequate blood supply to a particular organ or tissue, resulting in a decrease in oxygen and nutrient supply. It is commonly caused by a blockage or narrowing of the blood vessels supplying the affected area.
- Intimal hyperplasia =is the thickening of the innermost layer of a blood vessel as a complication of a reconstruction procedure.
- Mass effect = Mass effect is a phenomenon in which a focal lesion or contusion causes surrounding areas of brain tissue or brain structures to be compressed and injured due to the degree of space that leaking blood, cerebrospinal fluid, or edema takes up within the restricted skull space.
- Perforation = an injury to a vessel/a hole in a vessel or artery
- Pseudoaneurysm = a ”false“ aneurysm which can result from an injury to the vessel wall. Pseudoaneurysms typically occur because of trauma, such as a puncture or rupture of an artery during a medical procedure or an injury.
- Rupture = tearing or bursting of a blood vessel or aneurysm
- Space-occupying infarction = a type of stroke that develops extensive and acute swelling of the brain. This leads to the squeezing to adjacent and other vital areas of the brain to its space-occupying effect.
- Stenosis/ In-stent stenosis = narrowing of an artery, usually due to the buildup of plaque or the formation of scar tissue. In-stent stenosis is a condition in which a previously placed stent within a blood vessel becomes narrowed or blocked.
- Thrombosis/ In-stent thrombosis = complete or partial occlusion of a blood vessel by blood clot. A thrombosis within a stent is called in-stent thrombosis.
- Vasospasm = sudden vessel constriction

The undesirable effects and residual risks listed in Table 9 were identified in the literature on flow diverters in general and are well known and adequately addressed in the risk management. This table considers both procedure-related and product-related risks. The percentages of occurrence of an undesirable effect were determined on the basis of published literature data on the devices of the Neurovascular Flow Diverters (see Table 9 and page 50). Only publications in which an appropriate number of patients were treated were considered in order to avoid the percentage figures being biased by too small patient populations. In this case, the number was set at 50 patients. In some cases, it was not possible to comply with this figure because only articles with smaller populations were available. These figures are given in *italics*. In total, 34 publications

were included in which only the p64, the p48 MW (HPC) and p64 MW (HPC) were used. Case reports were excluded.

Table 9: Residual risks and undesirable effects of Neurovascular Flow Diverter devices, the percentages of occurrence and their reference in the literature.

Undesirable effects/Residual risk	Min. – Max. reported number [Reference]
Air Embolism	Not reported
Embolism in distal vessels	1/121 (0.8%) [5] - Not reported
Thrombosis	4/617 (0.6%) [6] - 2/121 (1.7%) [5]
In-stent thrombosis	4/1781 (0.2%) [7] - 2/79 (2.5%) [8]
Thromboembolism	2/1781 (0.1%) [7] - 3/74 (4.1%) [9]
(Transient) stenosis of target vessel	Not reported
In-stent stenosis (ISS)	1/1781 (0.06%) [7] - 16/84 (19%) [10]
Intimal hyperplasia	*5/22 (22.7%)* [11] - 29/108 (26.9%) [12]
Vasospasm	*3/48 (6.3%)* [13] - 9/84 (10.7%) [14]
Vessel occlusion	1/530 (0.2%) [6] - 1/121 (0.8%) [5]
Occlusion of side branch/perforator	2/420 (0.5%) [15] - 4/54 (7.4%) [16]
Cerebral ischemia	1/1781 (0.06%) [7] -4/54 (7.4%) [16]
Transient ischemic attack (TIA)	2/121 (1.7%) [5] - 3/100 (3%) [10]
Perforation	4/1781 (0.2%) [7] - 1/54 (1.9%) [16]
Rupture	1/1781 (0.05%) [7] - 1/100 (1%) [10]
Dissection	1/420 (0.2%) [15] - 1/54 (1.9%) [16]
Delayed aneurysm rupture	1/617 (0.2%) [6] - 1/72 (1.4%) [17]
Formation of a pseudoaneurysm	Not reported
Other arterial lesions	Not reported
Hemorrhage	1/420 (0.2%) [15] - 2/54 (3.7%) [16]
Bleeding	1/22 (4.5%) [11] - Not reported
Hematoma	1/530 (0.2%) [6] - 1/72 (1.4%) [17]
Hydrocephalus	Not reported
Stroke (ischemic and hemorrhagic)	1.1% [18] - 24/372 (6.4%) [15]
Infarction	1/530 (0.2%) [6] - 7/100 (7%) [10]
Neurological deficits	6/617 (0.3%) [6] - 11/79 (13.9%) [8]
Adverse reaction to antiplatelet/anticoagulation agents, anesthesia, radiation exposure	3/617 (0.5%) [6] - Not reported
Access site complications, e.g., groin hematoma	6/617 (1%) [6] - Not reported
Allergic reaction, infection	2/617 (0.3%) [6] - Not reported
Foreign body reaction	1/102 (1%) [19] - Not reported
Inflammation	1/79 (1.3%) [8] - *1/48 (2.1%)* [13]
Pain	Not reported
Edema	1/102 (1%) [19] - Not reported
Encephalopathy	Not reported
Extravasation	Not reported
Mass effect	2/617 (0.3%) [6] -Not reported
Persistent vegetative state	Not reported
Death	2/530 (0.4%) [6] - 1/54 (1.9%) [16]
Other	Not reported
Friction	Not reported
Inadequate apposition	*1/32 (3.1%)* [20] - Not reported
Unintentional release at an unplanned localization	*1/25 (4%)* [21] - Not reported
Detachment or deployment problems	3/617 (0.5%) [6] - 10/132 (7.6%) [19]
Incomplete opening	3/617 (0.5%) [6] - 4/108 (3.7%) [12]
Collapse	1/79 (1.3%) [8] - *1/29 (3.5%)* [22]

Undesirable effects/Residual risk	Min. – Max. reported number [Reference]
Fracture of implant and/or delivery system before or during the intervention§	Not reported
Separation failure§	Not reported
Migration	1/100 (1%) [10] - 1/54 (1.9%) [16]
Implant-Coil combination issues§	Not reported
Implant-implant combination issues§	Not reported
Implant-microcatheter combination issues§	Not reported
Deformation	*1/48 (2.1%)* [13] - 3/100 (3%) [10]
Resheathing problems	*1/7 (14.3%)* [23] - Not reported
(Fore)shortening	2/89 (2.2%) [14] - 8/100 (8%) [10]

Warnings and precautions

Concomitant medication

The antiplatelet medication is also known as " blood thinners" in everyday language. Non-compliance to the antiplatelet medication can lead to occlusion of the arteries followed by stroke. A treatment with p64, p48 MW (HPC) and p64 MW (HPC) is always accompanied with the antiplatelet medications as they prevent platelets from forming blood clots in the arteries. Blood clots can block the arteries and affect the blood supply leading to damage of the tissue supplied by that artery. **If you have any questions regarding the agents, please consult your doctor.**

Precautions

As per the Instructions For Use (IFU), the Neurovascular Flow Diverters are only conditionally compatible with magnetic resonance imaging *(= MRI; non-invasive medical imaging test that produces detailed images of almost every internal structure in the human body, including blood vessels)*. Non-clinical tests have shown that the flow modulation devices are suitable for MRI at a magnetic flux density of 3 Tesla. Under clinical conditions, 1.5 Tesla has proven to be unproblematic for the implant. **In case you have questions regarding this topic, please refer to your doctor/the treating doctor.**

Control visits (= follow-up visits)

To ensure your health condition and to prove the safety and performance of the Neurovascular Flow Diverters, control imaging visits are performed after treatment. Through these control visits, possible undesirable effects can be detected and treated. Furthermore, the progress and success of the treatment can be determined. The time frame for the control visits is scheduled individually by each hospital. The visit can for example include the assessment of your nervous system (= *neurological*) via the following grading scales:

- **mRS score** (modified Rankin Scale):
  The mRS (scale ranges from 0 - 6) is used to assess your/the patient's condition. The mRS indicates the degree of functional independence. If the mRS is evaluated before and after treatment, it can be determined whether the treatment has improved or worsened your/the patient's health condition or whether your/the patient's condition is unchanged.
- **NIHSS score** (National Institutes of Health Stroke Scale):
  The NIHSS score is a tool to systematically assess stroke-related neurologic deficits (= *abnormalities or impairments in the structure or function of the nervous system, which includes the brain, spinal*

cord, and nerves). The maximum possible score is 42 (i.e., death), with the minimum score being 0 (no stroke symptoms).

Summary of any field safety corrective action (FSCA including FSN)

Up until now, no safety measures had to be taken for p64, p48 MW (HPC) or p64 MW (HPC). For none of the devices so-called "field safety corrective actions" including "field safety notices" (abbreviation: FSCA and FSN) had to be performed. All devices are still being used by the doctors and none of the devices was retrieved from the market due to lack of safety. No serious incidents were reported.

5 Summary of clinical evaluation and post-market clinical follow-up

The following parts explain how the clinical safety and performance of the Neurovascular Flow Diverters are tracked and determined. Furthermore, the basis on which the clinical safety and performance of the Neurovascular Flow Diverters is established, is described.

Clinical background of the device

Flow diverters are not a fundamentally new technology on the market. In 2004, the term "flow divertor" was introduced into the lexicon by the author Lieber *et al.* [56, 57] In 2007, a new generation of endovascular devices was brought into the field of neurointervention termed "flow-disrupting" devices[58]. And in 2008, this technology was always referred to as "flow diverters" (abbreviation: FDs) due to different conducted studies e.g., the Pipeline for Uncoilable or Failed Aneurysms (PUFs) study [59]. Primary endovascular reconstruction with flow diverters became a main shift in the technique of endovascular aneurysm treatment.

The p64 Flow Modulation Device was CE (*Conformité Européenne* – European conformity) certified for the first time on 15.10.2012 (please refer to chapter 1). Numerous published case series and the "Diversion-p64" [24] study demonstrate its safety and effectiveness in real-world practice.

The p48 MW (HPC) Flow Modulation Device and the p64 MW (HPC) Flow Modulation Device are the further development of the p64. The p48 MW (HPC) Flow Modulation Device was CE (*Conformité Européenne* – European conformity) certified for the first time on 30.05.2018 (please refer to chapter 1) and the p64 MW (HPC) was certified for the first time on 22.12.2019 (please refer to chapter 1).

The clinical evidence for the CE-marking

The device variants p64, p48 MW (HPC) and p64 MW (HPC) have a CE-certification under the "Medical Device Directive" (MDD) and under the "Medical Device Regulation" (MDR).

No clinical study was conducted for the MDR-certification of p48/p64 MW (HPC) with the harmonized delivery system and p48 LITE (HPC), as sufficient clinical data was generated with the equivalent devices. Equivalence with respect to the technical, biological and clinical characteristics was demonstrated. p48 LITE (HPC) is considered equivalent to the existing p48 MW (HPC). The product variants with the new harmonized delivery system are considered equivalent to the existing variants of p48 MW (HPC) and p64 MW (HPC), respectively.

The collected data demonstrate that Neurovascular Flow Diverters are safe and effective for the treatment of e.g., aneurysms.

Clinical morbidity *(= the condition of suffering from a disease or medical condition)* and mortality *(= number of deaths)* rates are within acceptable limits for all patients treated with any of the Neurovascular Flow Diverter products. Own clinical data revealed stroke rates between 0% - 3.3% and the mortality rate varied between 0% - 1.5%. The Diversion-p64 study results, published by Bonafé *et al.*[24], report a low permanent morbidity and mortality of 2.4%. Yarahmadi *et al.* [29] performed a meta-analysis with similar flow diverters and reported permanent morbidity in 3.3% and mortality in 1.7% of patients.

In order to ensure the safe handling of the Neurovascular Flow Diverters during the treatment, the devices provide a good visibility during the treatment under X-ray (see Figure 12 and Figure 13).

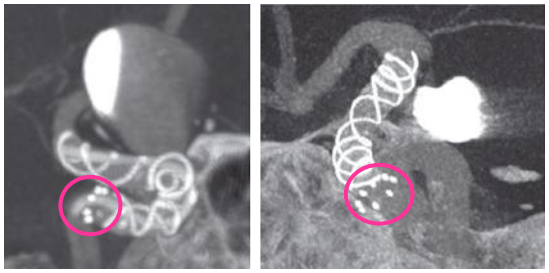


Figure 12: Visibility of the p64 flow diverter due to helical strands and eight markers (circle in pink). (Images taken from the officially available phenox brochure: https://phenox.net/international/uploads/KIF/p64_KIF-0008G_LR.pdf).

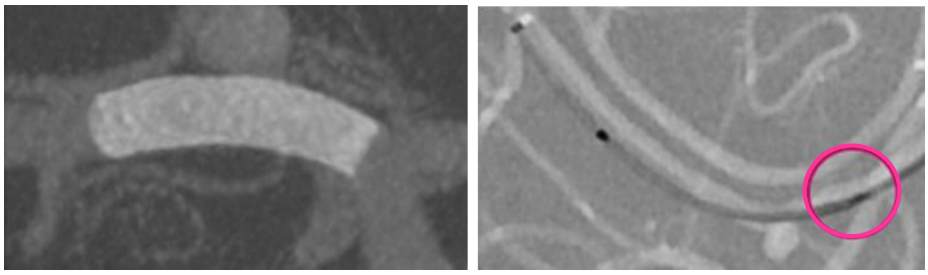


Figure 13: Optimal vessel wall apposition can be assessed more easily by the fully visible p64 MW (HPC) and p48 MW (HPC) resulting in more precise positioning. A radiopaque marker indicates the "point of no return" up to which the p64 MW (HPC) and p48 MW (HPC) can be pushed into the microcatheter (circle in pink). (Images taken from the officially available phenox brochure: https://phenox.net/international/uploads/KIF/pFMD-KIF-0057C_v2.pdf).

The X-ray visibility helps to avoid the situation that the devices are implanted in a wrong position.

The risks associated with the Neurovascular Flow Diverter implantation are listed in chapter 4 as also documented in the Instructions for Use (IFU) of the respective device. Complications that were found in the literature on p64, p48 MW (HPC) and p64 MW (HPC) are summarised in Table 9. There were no new risks found in the literature other than the ones already mentioned in Table 9 .

Further, as part of the so-called Post-Market Clinical Follow-Up *(= PMCF; market observation of the certified product)*, clinical data are proactively and systematically collected and analysed on the basis of the indications, contraindications and intended purpose of the Neurovascular Flow Diverters (please refer to chapter 2) to ensure the safe handling of the devices. This includes e.g., market feedback (e.g., in case doctors have claims regarding the handling of the product), literature analysis of phenox´ own products as well as literature and clinical data analysis regarding equivalent or similar devices and analysis of federal safety databases (e.g., from Germany: BfArM or the USA: FDA-MAUDE). Further to the methods and procedures named above, phenox initiated clinical studies are being performed. The aim of the COATING study (https://clinicaltrials.gov Identification number: NCT04870047) is intended to compare the safety and effectiveness of the coated p64 MW HPC under SAPT and uncoated p64 MW under DAPT.

The DART study is a randomized controlled study with the aim to evaluate the effectiveness and safety of the coated p48 MW HPC under DAPT and SAPT.
Further to this, phenox performed the "Diversion-p64" study (https://clinicaltrials.gov Identification number: NCT02600364) with the p64 Flow Modulation Device. The safety and efficacy of p64 was proven.

A critical assessment of the intended benefits of a treatment with these devices compared to the risks described in chapter 4, leads to the conclusion that the benefits clearly outweigh the identifiable risks. Based on this benefit-risk assessment and own clinical experience reported, it can be concluded that the p64, the p48 MW (HPC) and the p64 MW (HPC) Flow Modulation Devices are safe and effective.

6 Possible diagnostic or therapeutic alternatives

When considering alternative treatments, it is recommended to contact your healthcare professional who can take into account your individual situation.

General description of therapeutic alternatives

Several factors must be considered to identify the best treatment method, including aneurysm location, size, shape, patient´s age and medical history. For the treatment of aneurysms, currently the following alternative treatment methods are available:

Observation:
Observation consists of routine periodic control imaging and doctor visits to have a look at your/the patient's aneurysm status.

(Micro-) Surgical clipping:
Clipping of aneurysms requires the performance of a so-called "craniotomy" (= *surgical operation in which a bone flap is temporarily removed from the skull to access the brain*). A small MRI (= *Magnetic resonance imaging; a medical imaging technique used to produce detailed anatomical images*)-compatible clothespin-like metal clip is placed across the neck of the aneurysm as shown in Figure 14 to seal off the neck and, thus prevent blood from entering the aneurysm.

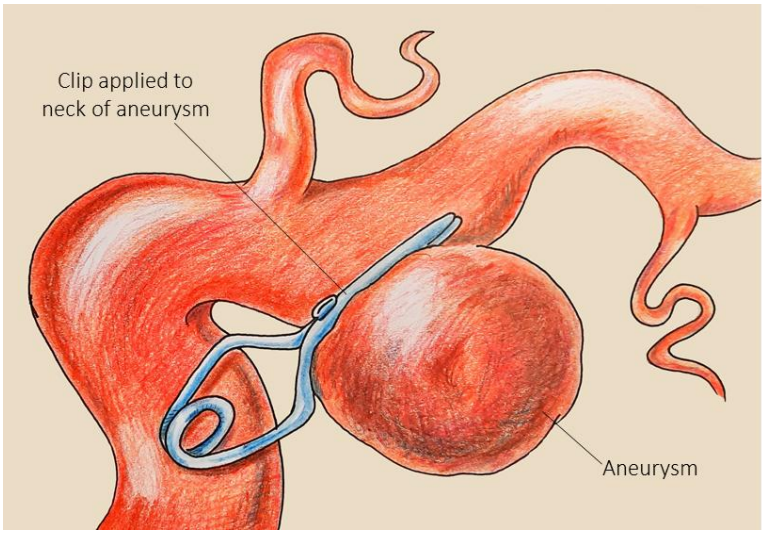


Figure 14: Application of a clip to the neck of an aneurysm. Drawing by Mark Hobert (phenox) and inspired by Brisman *et al.* (2006)[53].

Bypass surgery:

Aneurysm management can also be done via a bypass by performing the excisions of the lesion and recanalization of the inflow and outflow arteries, with or without grafting.

Coiling:

Endovascular (= *within the blood vessel*) management of aneurysms with detachable coils has been used since the early 1990s. Coils are detachable platinum wires, which are packed into the aneurysm to promote blood clotting and close off the aneurysm. Therefore, with the use of angiographic (= imaging, radiological procedure in which the vessels are filled with contrast medium and made visible with the help of X-rays, magnetic resonance tomography or computer tomography) techniques, a thin flexible tube (= microcatheter) is advanced into the aneurysm (see Figure 15). Once the catheter reaches the aneurysm, a coil is inserted which fills the aneurysmal sac as depicted in Figure 15. The coil is left in place permanently.

In complex aneurysm shapes, additional products, such as balloons and stents are used to prevent coil prolapse into the vessel. Balloon assisted coiling involves placement of a removeable balloon next to the aneurysm, which prevents coil prolapse into the supplying vessel. With stent-assisted coiling on the other hand, a stent is placed permanently in the vessel next to the aneurysm providing a scaffold for tissue development for aneurysm neck coverage.

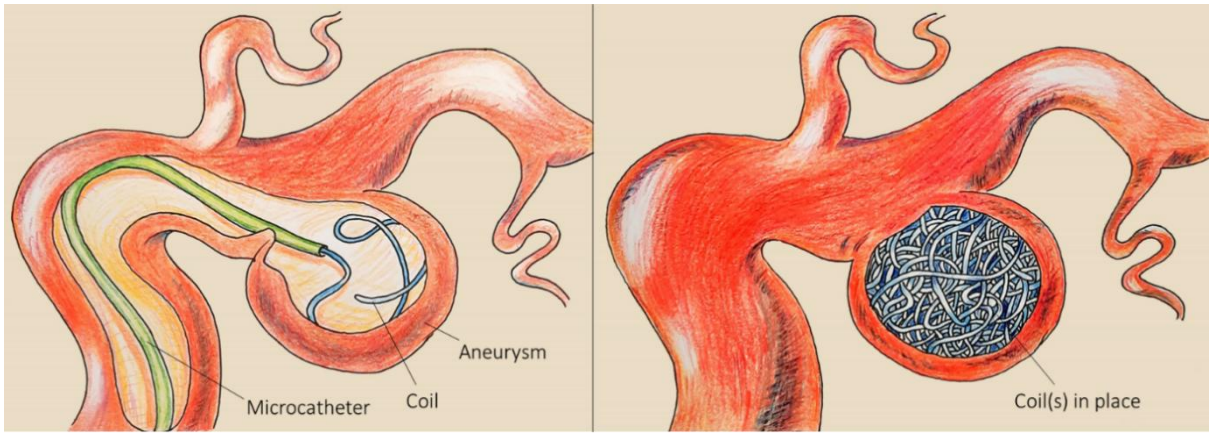


Figure 15: Procedure of coiling in treatment of aneurysmal malformation. Drawing by Mark Hobert (phenox) and inspired by Brisman *et al.* (2006)[53].

pCONUS Bifurcation Aneurysm Implant (phenox GmbH):

The products of the pCONUS product family (for example see pCONUS 1 in Figure 16) are used to treat bifurcation aneurysms (= *area where a vessel divides into two branches*) in combination with coils (= *thin threads mostly made of platinum*).

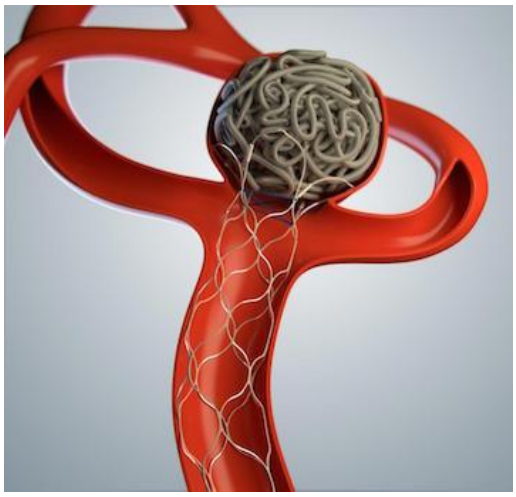


Figure 16: Schematic illustration of the pCONUS 1 (phenox GmbH)

Dissections can be treated through various approaches depending on the severity and location of the dissection. The treatment options include medical management, surgical therapy involving surgical bypass and clipping as well as endovascular therapy using minimally invasive techniques such as (stent-assisted) coiling or stent placement and flow diverter stents [46].
In case of recurring dissections despite medical treatment, endovascular treatment is considered a viable additional treatment alongside the anticoagulant medication. The Guidelines for Secondary Stroke Prevention recommend endovascular treatment in cases with definite recurring cerebral ischemic events [47]. There are examples of successful stent reconstruction of carotid dissections with acceptable immediate and long-term outcomes but further evaluation is needed [48].

The treatment for perforations involves directly sealing the perforation site with coils, liquid adhesives, a combination of both or balloon inflation. In the latter, a balloon is temporarily placed over the perforation site for several minutes, then deflated, and removed when no further extravasation is observed [49].

The guideline [50] recommends various treatment methods for arteriovenous malformations (AVMs), including neurointerventional, neurosurgical and radiotherapeutic therapy. Endovascular treatment options involve the injection of special materials, such as glue or tiny particles, or coils into the blood vessels feeding the AVM. This includes transarterial *(= refers to a medical procedure or device that is performed or inserted through an artery)* embolization with Onyx® *(= liquid non-adhesive viscous embolic agent)* and transvenous *(= refers to a medical procedure or device that is performed or inserted through a vein)* embolization using coils, which are well-established and have low complication rates. However, particle or tissue adhesive embolization is less controllable and rarely leads to permanent closure of the fistula, so it should not be routinely used. Coils are commonly used for transvenous embolization, and in some cases, liquid embolization can be introduced through venous probing of the fistula, possibly combined with coil treatment. Neurosurgical treatment involves identifying the exact location of the fistula point and eliminating it through coagulation, transection, or clipping. Stereotactic radiotherapy *(= specialized form of radiation*

therapy that aims to damage and eventually close off the abnormal blood vessels, reducing the risk of bleeding or other complications associated with the AVM) is another option, although it is rarely used and suitable for specific cases with circumscribed fistulas or high-risk patients.
In some cases, a combination of treatment approaches may be used.

Please contact your/the doctor, if you have questions regarding alternative treatment options.

7 Suggested training for users

The Neurovascular Flow Diverters may only be used in a (neuro-) radiological clinic by specialized, appropriately trained doctors who are experienced in the use of flow modulation devices. Participation in a product training course from phenox GmbH is recommended for the use of the product.

Publications

Publications on p64, p48 MW (HPC) and p64 MW (HPC)

All known publications regarding p64, p48 MW (HPC) and p64 MW (HPC) are listed below.

Table 10: Known publications about p64 Flow Modulation Device

Citation - p64 publications - status September 2024
Publications on only p64
Aguilar Perez, M., et al., *Endovascular Treatment of Anterior Circulation Aneurysms With the p64 Flow Modulation Device: Mid- and Long-Term Results in 617 Aneurysms From a Single Center.* Oper Neurosurg (Hagerstown), 2021. 20(4): p. 355-363.
Sirakov, S., et al., *The p64 Flow Diverter-Mid-term and Long-term Results from a Single Center.* Clin *Neuroradiol*, 2020. 30(3): p. 471-480.
Hellstern, V., et al., *Microsurgical clipping and endovascular flow diversion of ruptured anterior circulation blood blister-like aneurysms.* Interv Neuroradiol, 2018. 24(6): p. 615-623.
Aguilar Perez, M., et al., *In-stent Stenosis after p64 Flow Diverter Treatment.* Clin Neuroradiol, 2018. 28(4): p. 563-568.
Morais, R., et al., *Endovascular treatment of intracranial aneurysms with the p64 flow diverter stent: mid-term results in 35 patients with 41 intracranial aneurysms.* Neuroradiology, 2017. 59(3): p. 263-269.
Briganti, F., et al., *Mid-term and long-term follow-up of intracranial aneurysms treated by the p64 Flow Modulation Device: a multicenter experience.* J Neurointerv Surg, 2017. 9(1): p. 70-76.
Briganti, F., et al., *p64 Flow Modulation Device in the treatment of intracranial aneurysms: initial experience and technical aspects.* J Neurointerv Surg, 2016. 8(2): p. 173-80.
Fischer, S., et al., *Initial Experience with p64: A Novel Mechanically Detachable Flow Diverter for the Treatment of Intracranial Saccular Sidewall Aneurysms.* AJNR Am J Neuroradiol, 2015. 36(11): p. 2082-9.
Hellstern, V., et al., *Endovascular Treatment of Posterior Circulation Saccular Aneurysms With the p64 Flow Modulation Device: Mid-and Long-Term Results in 54 Aneurysms From a Single Center.* Front Neurol, 2021. 12: p. 711863.
De Beule, T., et al., *p64 flow diverter: Results in 108 patients from a single center.* Interv Neuroradiol, 2021. 27(1): p. 51-59.
Bonafe, A., et al., *Diversion-p64: results from an international, prospective, multicenter, single-arm post-market study to assess the safety and effectiveness of the p64 flow modulation device.* J Neurointerv Surg, 2022. 14(9): p. 898-903.
Publications on p64 and other phenox flow diverters
Vivanco-Suarez, J., et al., *Safety and efficacy of the p48 MW and p64 flow modulation devices: a systematic review and meta-analysis.* Neurosurg Focus, 2023. 54(5): p. E7.
Bilgin, C., et al., *Phenox HPC and Phenox flow modulation devices for the endovascular treatment of intracranial aneurysms: a systematic review and meta-analysis.* J Neurointerv Surg, 2024. 16(7): p. 706-714.
Hellstern, V., et al., *Flow diversion for unruptured MCA bifurcation aneurysms: comparison of p64 classic, p64 MW HPC, and p48 MW HPC flow diverter stents.* Frontiers in Neurology, 2024. 15.
Publication on p64 and similar flow diverters
Cagnazzo, F., et al., *Treatment of Unruptured Distal Anterior Circulation Aneurysms with Flow-Diverter Stents: A Meta-Analysis.* AJNR Am J Neuroradiol, 2019. 40(4): p. 687-693.
Zhou, G., et al., *Complications associated with the use of flow-diverting devices for cerebral aneurysms: a systematic review and meta-analysis.* Neurosurg Focus, 2017. 42(6): p. E17.
Gory, B., et al., *Flow Diverters for Intracranial Aneurysms: The DIVERSION National Prospective Cohort Study.* Stroke, 2019. 50(12): p. 3471-3480.
Bhogal, P., et al., *Treatment of Unruptured, Tandem Aneurysms of the ICA with a Single Flow Diverter.* Clin Neuroradiol, 2019. 29(4): p. 725-731.
Wendl, C.M., et al., *Direct carotid cavernous sinus fistulae: vessel reconstruction using flow-diverting implants.* Clin Neuroradiol, 2017. 27(4): p. 493-501.
Briganti, F., et al., *Postprocedural, midterm, and long-term results of cerebral aneurysms treated with flow-diverter devices: 7-year experience at a single center.* Neurosurg Focus, 2017. 42(6): p. E3.

Citation - p64 publications - status September 2024
Maybaum, J., et al., *Flow Diversion for Reconstruction of Intradural Vertebral Artery Dissecting Aneurysms Causing Subarachnoid Hemorrhage-A Retrospective Study From Four Neurovascular Centers.* Front Neurol, 2021. 12: p. 700164.
Narata, A.P., et al., *Reversible Brain Edema Associated with Flow Diverter Stent Procedures: A Retrospective Single- Center Study to Evaluate Frequency, Clinical Evolution, and Possible Mechanism.* World Neurosurg, 2019. 122: p. e569-e576.
Bhogal, P., et al., *Treatment of Unruptured, Saccular, Anterior Choroidal Artery Aneurysms with Flow Diversion : A Single Centre Experience.* Clin Neuroradiol, 2019. 29(3): p. 459-465.
Yaltirik Bilgin, E., et al., *Endovascular Treatment of Intracranial Anterior Circulation Aneurysms with Flow Diverters: A Single Centre Experience with mid and long-term results.* Turk Neurosurg, 2017.
Peschillo, S., et al., *Endovascular Treatment of Large and Giant Carotid Aneurysms with Flow-Diverter Stents Alone or in Combination with Coils: A Multicenter Experience and Long-Term Follow-up.* Oper Neurosurg (Hagerstown), 2017. 13(4): p. 492-502.
Bhogal, P., et al., *The Use of Flow Diverting Stents to Treat Para-Ophthalmic Aneurysms.* Front Neurol, 2017. 8: p. 381.
Bhogal, P., et al., *The Fate of Side Branches Covered by Flow Diverters-Results from 140 Patients.* World Neurosurg, 2017. 103: p. 789-798.
Bhogal, P., et al., *Flow Diversion for the Treatment of MCA Bifurcation Aneurysms-A Single Centre Experience.* Front Neurol, 2017. 8: p. 20.
Bhogal, P., et al., *Treatment of posterior circulation non-saccular aneurysms with flow diverters: a single-center experience and review of 56 patients.* J Neurointerv Surg, 2017. 9(5): p. 471-481.
Guzzardi, G., et al., *Long-term follow-up in the endovascular treatment of intracranial aneurysms with flow-diverter stents: update of a single-centre experience.* Radiol Med, 2018. 123(6): p. 449-455.
Bhogal, P., et al., *Management of Unruptured Saccular Aneurysms of the M1 Segment with Flow Diversion : A Single Centre Experience.* Clin Neuroradiol, 2018. 28(2): p. 209-216.
Giorgianni, A., et al., *Flow Diversion for Acutely Ruptured Intracranial Aneurysms Treatment: A Retrospective Study and Literature Review.* J Stroke Cerebrovasc Dis, 2022. 31(3): p. 106284.
Simgen, A., et al., *Endovascular treatment of unruptured intracranial aneurysms with flow diverters: A retrospective long-term single center analysis.* Neuroradiol J, 2023. 36(1): p. 76-85.
Khanafer, A., et al., *Endovascular treatment of distal anterior cerebral artery aneurysms using flow modulation devices: mid- and long-term results from a two-center study.* Front Neurol, 2024. 15: p. 1368612.
Abdel-Tawab, M., et al., *Efficacy and safety of flow diverters in posterior circulation aneurysms and comparison with their efficacy in anterior circulation aneurysms: A systematic review and meta-analysis.* Interv Neuroradiol, 2021. 27(5): p. 609-621.
Alwakeal, A., et al., *Flow Diversion of Posterior Circulation Aneurysms: Systematic Review of Disaggregated Individual Patient Data.* AJNR Am J Neuroradiol, 2021. 42(10): p. 1827-1833.

Table 11: Known publications about p48 MW (HPC) Flow Modulation Device

Citation - p48 MW (HPC) publications - status September 2024
Publications on only p48 MW
AlMatter, M., et al., *The p48 MW flow modulation device for treatment of unruptured, saccular intracranial aneurysms: a single center experience from 77 consecutive aneurysms.* CVIR Endovasc, 2020. 3(1): p. 39.
Bhogal, P., et al., *The p48MW Flow Diverter-Initial Human Experience.* Clin Neuroradiol, 2021. 31(1): p. 135-145.
Publications on p48 MW and other phenox flow diverters
Vivanco-Suarez, J., et al., *Safety and efficacy of the p48 MW and p64 flow modulation devices: a systematic review and meta-analysis.* Neurosurg Focus, 2023. 54(5): p. E7.
Bilgin, C., et al., *Phenox HPC and Phenox flow modulation devices for the endovascular treatment of intracranial aneurysms: a systematic review and meta-analysis.* J Neurointerv Surg, 2024. 16(7): p. 706-714.
den Bergh, F.V., et al., *The p48 flow diverter: First clinical results in 25 aneurysms in three centers.* Interv Neuroradiol, 2021. 27(3): p. 339-345.
Schob, S., et al., *Single-Center Experience With the Bare p48MW Low-Profile Flow Diverter and Its Hydrophilically Covered Version for Treatment of Bifurcation Aneurysms in Distal Segments of the Anterior and Posterior Circulation.* Front Neurol, 2020. 11: p. 1050.

Citation - p48 MW (HPC) publications - status September 2024
Publications on p48 MW and similar flow diverters
Dabhi, N., et al., *Flow Diverter Devices for Treatment of Intracranial Aneurysms in Small Parent Vessels-A Systematic Review of Literature.* World Neurosurg, 2022. 162: p. 183-194.e7.
Giorgianni, A., et al., *Flow Diversion for Acutely Ruptured Intracranial Aneurysms Treatment: A Retrospective Study and Literature Review.* J Stroke Cerebrovasc Dis, 2022. 31(3): p. 106284.
Khanafer, A., et al., *Endovascular treatment of distal anterior cerebral artery aneurysms using flow modulation devices: mid- and long-term results from a two-center study.* Front Neurol, 2024. 15: p. 1368612.
Publications on only p48 MW HPC
de Castro-Afonso, L.H., et al., *Treatment of distal unruptured intracranial aneurysms using a surface-modified flow diverter under prasugrel monotherapy: a pilot safety trial.* J Neurointerv Surg, 2021. 13(7): p. 647-651.
de Castro-Afonso, L.H., et al., *Aspirin monotherapy in the treatment of distal intracranial aneurysms with a surface modified flow diverter: a pilot study.* J Neurointerv Surg, 2021. 13(4): p. 336-341.
Bhogal, P., et al., *The p48_HPC antithrombogenic flow diverter: initial human experience using single antiplatelet therapy.* J Int Med Res, 2020. 48(1): p. 300060519879580.
Aguilar-Perez, M., et al., *The p48 Flow Modulation Device with Hydrophilic Polymer Coating (HPC) for the Treatment of Acutely Ruptured Aneurysms: Early Clinical Experience Using Single Antiplatelet Therapy.* Cardiovasc Intervent Radiol, 2020. 43(5): p. 740-748.
Pierot, L., et al., *Surface-modified flow diverter p48-MW-HPC: Preliminary clinical experience in 28 patients treated in two centers.* J Neuroradiol, 2021. 48(3): p. 195-199.
de Castro-Afonso, L.H., et al., *Two year follow-up of distal unruptured intracranial aneurysms treated with a surface modified flow diverter under prasugrel monotherapy.* J Neurointerv Surg, 2023.
Publications on p48 MW HPC and other phenox flow diverters
Vivanco-Suarez, J., et al., *Safety and efficacy of the p48 MW and p64 flow modulation devices: a systematic review and meta-analysis.* Neurosurg Focus, 2023. 54(5): p. E7.
Bilgin, C., et al., *Phenox HPC and Phenox flow modulation devices for the endovascular treatment of intracranial aneurysms: a systematic review and meta-analysis.* J Neurointerv Surg, 2024. 16(7): p. 706-714.
Lobsien, D., et al., *Aneurysm Treatment in Acute SAH with Hydrophilic-Coated Flow Diverters under Single-Antiplatelet Therapy: A 3-Center Experience.* AJNR Am J Neuroradiol, 2021. 42(3): p. 508-515.
Guzzardi, G., et al., *Flow diverter stents with hydrophilic polymer coating for the treatment of acutely ruptured aneurysms using single antiplatelet therapy: Preliminary experience.* Interv Neuroradiol, 2020. 26(5): p. 525-531.
Bhogal, P., et al., *Early clinical experience with the p48MW HPC and p64MW HPC flow diverters in the anterior circulation aneurysm using single anti-platelet treatment.* Interv Neuroradiol, 2022. 28(3): p. 266-276.
Khanafer, A., et al., *Flow diversion with hydrophilic polymer coating with prasugrel as single antiplatelet therapy in the treatment of acutely ruptured intracranial aneurysms: a multicenter case series, complication and occlusion rates.* J Neurointerv Surg, 2024.
den Bergh, F.V., et al., *The p48 flow diverter: First clinical results in 25 aneurysms in three centers.* Interv Neuroradiol, 2021. 27(3): p. 339-345.
Schob, S., et al., *Single-Center Experience With the Bare p48MW Low-Profile Flow Diverter and Its Hydrophilically Covered Version for Treatment of Bifurcation Aneurysms in Distal Segments of the Anterior and Posterior Circulation.* Front Neurol, 2020. 11: p. 1050.
Hellstern, V., et al., *Flow diversion for unruptured MCA bifurcation aneurysms: comparison of p64 classic, p64 MW HPC, and p48 MW HPC flow diverter stents.* Frontiers in Neurology, 2024. 15.
Publications on p48 MW HPC and similar flow diverters
Ma, L., et al., *Flow Diverters with Surface Modification in Patients with Intracranial Aneurysms: A Systematic Review and Meta-Analysis.* World Neurosurg, 2024. 185: p. 320-326.e17.
Schüngel, M.S., et al., *Distal Flow Diversion with Anti-Thrombotically Coated and Bare Metal Low-Profile Flow Diverters-A Comparison.* J Clin Med, 2023. 12(7).
Gawlitza, M., et al., *A Systematic Literature Review and Meta-Analysis of the Treatment of Ruptured Intracranial Aneurysms with Hydrophilic Polymer and Phosphorylcholine-Coated Flow Diverters Under Single Antiplatelet Therapy.* World Neurosurg, 2023. 170: p. e791-e800.

Citation - p48 MW (HPC) publications - status September 2024
Monteiro, A., et al., *Treatment of ruptured intracranial aneurysms using the novel generation of flow-diverters with surface modification: A systematic review and meta-analysis.* Interv Neuroradiol, 2024. 30(3): p. 350-360.
Maybaum, J., et al., *Flow Diversion for Reconstruction of Intradural Vertebral Artery Dissecting Aneurysms Causing Subarachnoid Hemorrhage-A Retrospective Study From Four Neurovascular Centers.* Front Neurol, 2021. 12: p. 700164.
Schungel, M.S., et al., *Endovascular Treatment of Intracranial Aneurysms in Small Peripheral Vessel Segments-Efficacy and Intermediate Follow-Up Results of Flow Diversion With the Silk Vista Baby Low-Profile Flow Diverter.* Front Neurol, 2021. 12: p. 671915.
Senol, Y.C., et al., *The safety profile of single antiplatelet therapy with flow diverters: Systematic review and meta-analysis.* Interv Neuroradiol, 2023: p. 15910199231168669.
Goertz, L., et al., *Safety and efficacy of coated flow diverters in the treatment of ruptured intracranial aneurysms: a retrospective multicenter study.* J Neurointerv Surg, 2024.
Khanafer, A., et al., *Endovascular treatment of distal anterior cerebral artery aneurysms using flow modulation devices: mid- and long-term results from a two-center study.* Front Neurol, 2024. 15: p. 1368612.

Table 12: Known publications about p64 MW (HPC) Flow Modulation Device

Citation- p64 MW (HPC) publications - status September 2024
Publications on only p64 MW HPC
Winters, H., et al., *First Experience of Three Neurovascular Centers With the p64MW-HPC, a Low-Profile Flow Diverter Designed for Proximal Cerebral Vessels With Antithrombotic Coating.* Front Neurol, 2021. 12: p. 724705.
Petrov, A., et al., *Initial experience with the novel p64MW HPC flow diverter from a cohort study in unruptured anterior circulation aneurysms under dual antiplatelet medication.* Interv Neuroradiol, 2021. 27(1): p. 42-50.
Hellstern, V., et al., *Use of a p64 MW Flow Diverter with Hydrophilic Polymer Coating (HPC) and Prasugrel Single Antiplatelet Therapy for the Treatment of Unruptured Anterior Circulation Aneurysms: Safety Data and Short-term Occlusion Rates.* Cardiovasc Intervent Radiol, 2022. 45(9): p. 1364-1374.
Ernst, M., et al., *Multicenter study of the safety and effectiveness of intracranial aneurysm treatment with the p64MW-HPC flow modulation device.* Interv Neuroradiol, 2023: p. 15910199231220964.
Publications on p64 MW HPC and other phenox flow diverters
Vivanco-Suarez, J., et al., *Safety and efficacy of the p48 MW and p64 flow modulation devices: a systematic review and meta-analysis.* Neurosurg Focus, 2023. 54(5): p. E7.
Bilgin, C., et al., *Phenox HPC and Phenox flow modulation devices for the endovascular treatment of intracranial aneurysms: a systematic review and meta-analysis.* J Neurointerv Surg, 2024. 16(7): p. 706-714.
Lobsien, D., et al., *Aneurysm Treatment in Acute SAH with Hydrophilic-Coated Flow Diverters under Single-Antiplatelet Therapy: A 3-Center Experience.* AJNR Am J Neuroradiol, 2021. 42(3): p. 508-515.
Guzzardi, G., et al., *Flow diverter stents with hydrophilic polymer coating for the treatment of acutely ruptured aneurysms using single antiplatelet therapy: Preliminary experience.* Interv Neuroradiol, 2020. 26(5): p. 525-531.
Bhogal, P., et al., *Early clinical experience with the p48MW HPC and p64MW HPC flow diverters in the anterior circulation aneurysm using single anti-platelet treatment.* Interv Neuroradiol, 2022. 28(3): p. 266-276.
Khanafer, A., et al., *Flow diversion with hydrophilic polymer coating with prasugrel as single antiplatelet therapy in the treatment of acutely ruptured intracranial aneurysms: a multicenter case series, complication and occlusion rates.* J Neurointerv Surg, 2024.
Hellstern, V., et al., *Flow diversion for unruptured MCA bifurcation aneurysms: comparison of p64 classic, p64 MW HPC, and p48 MW HPC flow diverter stents.* Frontiers in Neurology, 2024. 15.
Publications on p64 MW HPC and similar flow diverters
Ma, L., et al., *Flow Diverters with Surface Modification in Patients with Intracranial Aneurysms: A Systematic Review and Meta-Analysis.* World Neurosurg, 2024. 185: p. 320-326.e17.
Gawlitza, M., et al., *A Systematic Literature Review and Meta-Analysis of the Treatment of Ruptured Intracranial Aneurysms with Hydrophilic Polymer and Phosphorylcholine-Coated Flow Diverters Under Single Antiplatelet Therapy.* World Neurosurg, 2023. 170: p. e791-e800.

Citation- p64 MW (HPC) publications - status September 2024
Monteiro, A., et al., *Treatment of ruptured intracranial aneurysms using the novel generation of flow-diverters with surface modification: A systematic review and meta-analysis.* Interv Neuroradiol, 2024. 30(3): p. 350-360.
Senol, Y.C., et al., *The safety profile of single antiplatelet therapy with flow diverters: Systematic review and meta-analysis.* Interv Neuroradiol, 2023: p. 15910199231168669.
Goertz, L., et al., *Safety and efficacy of coated flow diverters in the treatment of ruptured intracranial aneurysms: a retrospective multicenter study.* J Neurointerv Surg, 2024.
Khanafer, A., et al., *Endovascular treatment of distal anterior cerebral artery aneurysms using flow modulation devices: mid- and long-term results from a two-center study.* Front Neurol, 2024. 15: p. 1368612.

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