ENGINEERING STROKE SOLUTIONS

Summary of Safety and Clinical Performance:

NeuroSpeed® PTA Balloon Catheter

Acandis GmbH

Summary of Safety and Clinical Performance according to Medical Device Regulation (MDR) EU 2017/745

Identifier: 2000

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1 Information for the professional user

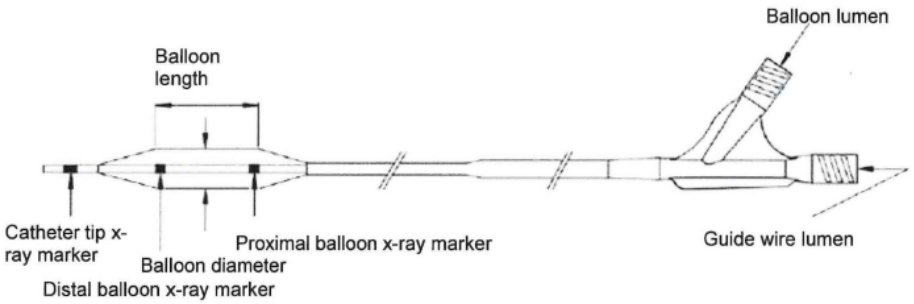
This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the NeuroSpeed® PTA Balloon Catheter.

The SSCP is prepared in accordance with the Medical Device Regulation (EU) 2017/745 (MDR) and the document MDCG 2019-9, Rev.1 from March 2022.

The SSCP is not intended to replace the instructions for use (IFU) as the main document to ensure the safe use of the NeuroSpeed® PTA Balloon Catheter nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.

The following information is intended for users/healthcare professionals.

1.1 Device identification and general information

Device trade name(s)	NeuroSpeed® PTA Balloon Catheter Article no. 01-000600, 01-000601, 01-000602, 01-000603, 01-000604, 01-000605 01-000610, 01-000611, 01-000612, 01-000613, 01-000614, 01-000615
Picture	
Manufacturer's name and address	Acandis GmbH, Theodor-Fahrner-Straße 6, 75177 Pforzheim, Germany
Manufacturer's single registration number (SRN)	DE-MF-000006259
Basic UDI-DI	426065033NeuroSpeedNR
Medical device nomenclature	– UMDNS: 17-184 Catheters, angioplasty, balloon dilatation – GMDN 17184 Peripheral angioplasty balloon catheter, basic – EMDN: C010499 Anqiography and Hemodynamics Devices - Other
Class of device	Class III medical product, as defined in Medical Device Regulation (MDR) EU 2017/745 Annex VIII, classification rule 7, bullet point 2
Year of first CE certificate	2014
Authorised representative	Not applicable
Notified body	DQS Medizinprodukte GmbH (Notified body number: 0297).

1.2 Intended use of the device

Intended purpose	The NeuroSpeed® PTA Balloon Catheter is intended for the dilation of intracranial arteries for improving perfusion. The NeuroSpeed® PTA Balloon Catheter is intended for the delivery of the self-expanding CREDO® Stent/CREDO® heal Stent. Please observe the instructions for use of the CREDO® Stent/CREDO® heal Stent.
Indication(s)	The NeuroSpeed® PTA Balloon Catheter is indicated for the treatment of intracranial stenosis.
Targeted population(s)	Intended user: The NeuroSpeed® PTA Balloon Catheter should be applied only by physicians who have the necessary background knowledge and experience in the field of percutaneous transluminal angioplasty (PTA).
	Patient target group: No special patient populations defined but patients with contraindications are to be excluded.
Contraindications and/or limitations	Usage is contraindicated for the following patients: – Patients in whom it is assumed that effective angioplasty of the lesion cannot be performed. – Patients in whom treatment with antiplatelet agents and/or anticoagulants is contraindicated. – Patients who present in the angiography with anatomical conditions unsuitable for endovascular treatment due to severe vessel tortuosity. General contraindications in connection with endovascular and/or angiographic treatments must be taken into consideration. No limitations are mentioned in the IFU

1.3 Device description

The NeuroSpeed® PTA Balloon Catheter is an over-the-wire coaxial catheter with a balloon near the distal tip for percutaneous transluminal angioplasty (PTA). The catheter dimensions and balloon sizes are specified on the packaging label. The balloon diameters at the corresponding pressure values can be seen in the compliance chart. The PTA balloon catheter has X-ray markers that simplify placement under fluoroscopy. One X-ray marker identifies the catheter tip, while two further X-ray markers identify the nominal length of the balloon. There are two Luer connections at the proximal end of the catheter: the central lumen for guiding the guide wire and a lateral lumen for inflating and deflating the balloon. The outer surface of the catheter has a hydrophilic coating for improved lubricity.

Sizes	Balloon diameters: 1.5 / 2.0 / 2.5 / 3.0 / 3.5 / 4.0 mm Balloon length: 8 mm / 15 mm Usable length: 150 cm
Sterility	Yes, for single-use

Stent placement after Balloon PTA possible without changing the catheter.

Insertion of the catheter using a suitable guide wire and appropriate accessories (such as guide catheter, sheath, hemostatic valves, infusion bags, etc.) to safely reach the target zone for a controlled placement in the middle of the stenosis, inflation of the balloon with a manometer and for delivery of the CREDO® (heal) stent.

1.3.1 Previous generations

The first generation has been on the market since May 2014, the second generation (range extension) since December 2015, the third generation (optimization components and process) since October 2018. The current generation of the NeuroSpeed® PTA Balloon Catheter (range extension new length 15 mm) is in development.

1.3.2 Accessories

No accessories

1.3.3 Combination with other devices

Compatible with inflation pump, standard guide wire, RHV (rotating hemostatic valve), lockable vacuum syringe, guiding catheter/sheath and compatible with CREDO® (heal) Stent.

1.4 Risks and warnings

1.4.1 Residual risks and undesirable effects

Possible complications, among others, include the following:

- General complications in connection with endovascular and/or angiographic treatments (e.g. (Intracerebral) hemorrhage, Embolism (air, foreign body, plaque or thrombus), Fever, Vessel dissection, Vessel perforation, Vessel rupture, Hyperperfusion syndrome, Infection, (Cerebral) ischemia/infarction, Secondary hemorrhage, Reactions due to radiation exposure, Subarachnoid hemorrhage, Thromboembolic event/stroke, Vasospasm, Intoxication)
- General complications in connection with thrombocyte aggregation inhibitors/ anticoagulants, anesthetics and contrast agents (e.g. Renal insufficiency)
- Complications in connection with vessel entry (e.g. Hematoma or bleeding at puncture site, Pain and/or infection at puncture site)
- Possible problems during catheter delivery (e.g. Balloon failure, Catheter breakage, Incorrect catheter placement, Catheter cannot be withdrawn, Catheter bending, Catheter compression, Catheter damage, Therapeutic or diagnostic aids cannot be used, Delayed treatment, Target area inaccessible or cannot be accessed safely)

- Other complications in connection with the catheter (e.g. Allergic reactions to the catheter material, (Distal) embolization including previously unaffected areas, (Re)stenosis)
- Neurological deficits (e.g. Dysphasia, Hemiparesis, Hemiplegia, Impaired vision, Oculomotor paresis, Speech disorders)
- Death

In the scientific literature, the most common complication is intracranial haemorrhage. Symptomatic intracranial haemorrhage occurred in 4 % (Stracke et al. 2020b) and 9.1 % (Stracke et al. 2020a), asymptomatic intracranial haemorrhage in 5.2 % (Meyer et al. 2020). One publication (Meyer et al. 2020) described peri-procedural stroke (6.5 %), in-stent restenosis (25 %), stroke recurrence (1.7 %) and stroke-related deaths (2.6 %) as well as two non-stroke related deaths (2.6 %). In one publication, no complications were observed (Möhlenbruch et al. 2016). Three device-related complications (two with CREDO, one with NeuroSpeed) were observed in the ASSISTENT PMCF study. In total, 7.7 % of the patients experienced a symptomatic and 7.7 % an asymptomatic intracranial haemorrhage. There were two deaths (7.7 %). Stroke rates were divided into non-disabling in the region of the target vessel (3.9 %), non-disabling outside the region of the target vessel (0 %), disabling in the region of the target vessel (7.7 %) and disabling outside the region of the target vessel (3.9 %). There were no cases of ischemic stroke. TIA occurred in 3.9 %. Symptomatic intracranial haemorrhage within 18 – 36 hours and device-related procedural complications were observed in 27.8 % (9.7 % – 53.5 %; per protocol population n = 18) each. In the full analysis set population (n = 19), the corresponding values for these endpoints are 26.3 % (9.1 % – 51.2 %). Calculations correspond to non-missing values. No dissections, perforations/ruptures of the target vessel, embolisms, stent migration or embolization in new territories were observed. The SICH rate was 26.3 %. Two stent thromboses occurred (10.5 % in the full-set analysis (n = 19) or 11.1 % in the per protocol population (n = 18) respectively). Parenchymal haemorrhage type 2 (PH-2) after 18 – 36 hours occurred in one patient (5.6 % (0.1 % – 27.3 %)). Two patients had an embolization in new territories (11.1% (1.4 % – 34.7 %)) and nine patients died or had a dependency (mRS 4 – 6) within 90 (± 10) days after stroke (35.3 % (14.2 % – 61.7 %); per protocol population n = 18). In the full analysis set (n = 19), this corresponds to 33.3 % (13.3 % – 59.0 %). A total of 6 patients died within 90 (± 10) days. In none of the patients, ischemic stroke in a downstream territory of the occluded vessel occurred within 90 (± 10) days after stroke (per protocol analysis, n = 18 and full analysis set n = 19). Calculations correspond to non-missing values. The overall mortality within the 27 patients was 33 %.

Mortality rates vary between the included publications. Similarly to that, Stracke et al. described a 90-day mortality of 17.1 % (Stracke et al. 2020b) and 18.5 % (Stracke et al. 2020a) after rescue stenting. Diana et al. reported that mortality was seen in 25 % (Diana et al. 2021).

In the ACUTE trial, the overall mortality within the 27 patients was 33 %. After 90 (± 10) days the mortality was 35.3 % in the per protocol population. This is higher than in the scientific literature on rescue stenting after failed mechanical thrombectomy. This could be partially due to the higher mean/median age in the ACUTE trial (68.2 ± 13.2 years / 71 (58.8, 79.5 years) compared to the that described in literature (median: 67 (59 – 75) years; Stracke et al. 2020a; 71 (61 – 79) years, Stracke et al. 2020b).

1.4.2 Warnings and precautions

Warnings

- The NeuroSpeed PTA Balloon Catheter should be applied only by physicians who have the necessary background knowledge and experience in the field of percutaneous transluminal angioplasty (PTA).
- No specific patient populations have been defined but patients with contraindications are to be excluded.
- Because application of the PTA balloon catheter involves the risk of subacute thrombosis, vascular complications and/or hemorrhages, it is necessary to select patients with care.
- Before use, the product needs to be carefully checked to ensure there is no transportation damage. Under no circumstances should damaged or kinked catheters be used.
- On no account whatsoever should you continue advancing the catheter if you encounter resistance without first finding out the cause, as otherwise you could damage the catheter or perforate the vessel.
- Intraluminal instruments must never be moved against resistance within the catheter. The application of too much force against resistance may lead to damage (e.g. cracks/ruptures) to the instrument and/or the catheter or injury to the vessel wall.
- Compatibility of the NeuroSpeed PTA Balloon Catheter with liquid embolizates cannot be guaranteed. It is not suitable for liquid embolizates based on cyanoacrylate and dimethylsulphoxide (DMSO).
- A corresponding treatment with anticoagulant and antiplatelet agents must be performed in accordance with well-established medical standards.
- The product may only be used for the intended purpose. Any use of the product for other purposes (off-label use) may lead to a deterioration in the patient's state of health or even their death.

Precautions

- The product is provided sterile and for single use only.

- In case of damage to the sterile barrier, the product must not be used. If any damage is visible, please contact your Acandis representative.
- Do not use the product after the expiration date printed on the label.
- Do not reuse, reprocess or resterilise. Reuse, reprocessing or resterilisation may compromise structural integrity of the components and/or lead to failure that, in turn, may result in complications, patient injury or death. Reuse, reprocessing or resterilising the device also increases the risk of contamination of the device and/or causes patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient.
- The hydrophilic coating of the outer surface of the catheter must be kept hydrated to maintain its lubricious properties.
- Once the catheter is inside the body, it should only be moved under fluoroscopy. Do not remove the catheter without checking how the tip reacts.
- The manufacturers' instructions for use should be observed for all materials used together with the PTA balloon catheter.

1.4.3 Other relevant aspects of safety

The complaint rate is 0.46 % and the incident rate is 0.06 % for the last four years. The medical benefit continues to outweigh the residual risk.
There were no FSNs or FSCAs in the last four years. In April 2017, there was a voluntary medical device recall of the affected batch due to a leakage at the Luer hub.

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

1.5.1 Summary of clinical data related to equivalent devices

No clinical data of equivalent devices from other manufacturers were used for the clinical evaluation.

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

No clinical data from proprietary investigations before CE-marking are available.

1.5.3 Summary of clinical data from other sources

1.5.3.1 Clinical data in the literature on the NeuroSpeed® PTA Balloon Catheter in combination with CREDO® / CREDO® heal Stent

Table 1: Study details and (ICS = intracranial atherosclerotic stenosis, TIA = transient ischemic stroke, ICA = intracranial atherosclerosis, VA = vertebral artery, BA = basilar artery)

Author	Study design	# of patients	Used devices	Indications	Location of stenosis
Bhogal et al. 2022	Case series: retrospective review of prospectively maintained database	24	NeuroSpeed: n = 1 2 x 15 mm	Angioplasty after fish-mouthing of the p64 HPC flow diverter	M1 (n = 1)
Buonomo et al. 2021	Case series	10	NeuroSpeed: n = 7	Acute ischemic stroke or TIA	BA (n = 4) ICA (n = 2) VA (n = 1) (PTA patients)
Diana et al. 2021	Case report	1	NeuroSpeed 2.5 x 8 mm with CREDO 4 x 15 mm	Intracranial angioplasty and stenting in patients with high ischemic stroke risk.	ICA siphon
Papa et al. 2020	Case report (Conference abstract)	3	NeuroSpeed PTA Balloon Catheter with Neuroform (n = 1) CREDO Stent (n = 2)	Recurrent TIA or stroke after failure of best medical treatment	Not mentioned.
Nordmeyer et al. 2019	Case series (Poster abstract)	17	NeuroSpeed PTA Balloon Catheter with CREDO heal	Initial large vessel occlusion and suspected underlying stenosis < 24 h after symptom onset. Rescue stenting was indicated in seven cases, in eight cases, symptomatic ICAD were treated.	Not further specified.
Giang et al. 2022	Case report	1	NeuroSpeed PTA Balloon Catheter 2.0 x 8 mm Jade balloon (OrbusNeich) 3.5 x 80 mm	Minor ischemic stroke resulting in right hemiparesis	Ipsilateral internal carotid artery stenosis

Table 2: Outcome parameters of pivotal clinical data (mRS = modified Rankin Scale, NIHSS = National Institutes of Health Stroke Scale, mENR = major early neurological recovery, sICH = symptomatic intracranial hemorrhage, ICS = intracranial atherosclerotic stenosis, eICS = elective intracranial stenting, FBTS = first balloon then stent, SAE = serious adverse event, n.a. = not applicable)

Author	Technical success	Pre-procedural stenosis	Post-procedural stenosis	Neurological outcome	Complications	Conclusion on safety and performance
Bhogal et al. 2022	100 %	n.a.	n.a.	mRS ≤ 1 n = 24	None	Fish-mouthing appearance was significantly improved with the NeuroSpeed, with good flow through the device and no complications
Buonomo et al. 2021	100 %	85.4 % (PTA patients)	54.4 % (PTA patients)	mRS ≤ 2: n = 7 (PTA patients) NIHSS improved from 8.7 ± 12.4 to 5 ± 9.79 (mean)	None	Intracranial stenosis endovascular treatment with Neuroform Atlas stent provides encouraging results, with or without the use of NeuroSpeed.
Diana et al. 2021	significant	-	-	mRS 1	Seizures, respiratory failure, cerebral hyperperfusion syndrome, no procedural complications	Cerebral hyperperfusion syndrome is a severe and underestimated complication of intracranial artery stenosis.
Papa et al. 2020	100 %	> 75 %	-	Not assessed	No complications	Clinical and angiographic results were encouraging. More data are mandatory to confirm the clinical benefit of endovascular treatment of intracranial stenosis.
Nordmeyer et al. 2019	TICI ≥ 2b = 82.3 %	Not assessed	Not assessed	Not assessed	One device-related complication (not further specified)	The CREDO heal Stent is a promising treatment option for patients with symptomatic ICAD or with persistent vascular occlusion. The final TICI sore is in accordance with uncoated devices. Its effectiveness regarding long-term ischemic complication has to be further evaluated.
Giang et al. 2022	No (first attempt with Neuro-Speed) 100 % with second intervention	Not assessed	Not assessed	After second intervention: mRS 1 3 months after discharge	After first intervention: Hemiplegia, increase in hypertense lesions in the left hemisphere, near occlusion in the left internal carotid artery Second intervention: none	With the first intervention using the NeuroSpeed PTA Balloon Catheter, the the stent could not reach the stenosis site due to the presence of a tortuous type III aortic arch in the left CCA. In a second approach, a transcervical approach instead of the transfemoral was used and succeeded.

Author	Technical success	Pre-procedural stenosis	Post-procedural stenosis	Neurological outcome	Complications	Conclusion on safety and performance
						No conclusions on the safety and performance of the NeuroSpeed PTA Balloon Catheter were drawn.

Most of the trials evaluated the safety and performance of the procedure in general or the additionally used stents, Therefore, only limited information on NeuroSpeed® PTA Balloon Catheter-related endpoints alone could be extracted from these publications.

1.5.3.2 Clinical data in the literature on the NeuroSpeed® PTA Balloon Catheter in combination with the ACCLINO (flex) Stent

Remark: According to the instructions for use, the NeuroSpeed® PTA Balloon Catheter is intended for the delivery of the CREDO® Stent/CREDO® heal Stent. Hence, the use together with the ACCLINO (flex) Stent is off-label.

Table 3: Study details and (ICS = intracranial atherosclerotic stenosis, TIA = transient ischemic stroke, ICA = intracranial atherosclerosis, VA = vertebral artery, BA = basilar artery)

Author	Study design	# of patients	Used devices	Indications	Location of stenosis
Möhlenbruch et al. 2016	Case series: Retrospective review of prospectively collected database	6	NeuroSpeed: 4 x 2 x 8 mm 1 x 3.5 x 8 mm 1 x 4 x 8 mm with ACCLINO Flex Stent	1) failure of dual antiplatelet therapy defined as recurrent TIA or ischemic stroke 2) presence of ICS of ≥ 70 % 3) endovascular accessibility of the target lesion as judged by CT angiography or MRI angiography	V4 (n = 3) M1 (n = 2) supraclinoid portion of the ICA (n = 1)
Stracke et al. 2020b	Case series: retrospective review	50	NeuroSpeed with ACCLINO (flex)	Bailout stenting for acute ischemic stroke after failed thrombectomy	M1 (n = 17) M2 (n = 1) VA (n = 10) BA (n = 14)

Author	Study design	# of patients	Used devices	Indications	Location of stenosis
Meyer et al. 2020	Case series: multi-center cohort study	76	NeuroSpeed: n = 58 Microcatheters n = 18 with ACCLINO (flex) Stent	Secondary stroke prevention in patients with symptomatic intracranial stenosis due to 1) Recurrent stroke 2) TIA	Terminal internal carotid artery (n = 21) M1 (n = 17) M2 (n = 2) Anterior cerebral artery (n = 2) V4 (n = 23) BA (n = 11)
Stracke et al. 2020a	Clinical study: retrospective analysis	61	NeuroSpeed Microcatheters with ACCLINO (flex) Stent	Bailout stenting for acute ischemic stroke after failed thrombectomy	ICA M1 M2 VA BA (Numbers not separated for different stent types used)
Capirossi et al. 2022	Case report	1	NeuroSpeed 4.0 x 8 mm with ACCLINO flex HRF 5.0 x 25 mm	Symptomatic right carotid syphon stenosis; one month earlier there was a minor stroke with left hemiparesis.	Right carotid syphon
Borota et al. 2022	Case report	1	NeuroSpeed PTA Balloon Catheter with ACCLINO HRF 3 x 20 mm	Wake-up stroke with basilar artery occlusion caused by spontaneous dissection in a 15-year-old	Basilar artery at the level of the anterior inferior cerebellar arteries

The ACCLINO® flex Stent obtained CE marking in February 2014 and has been developed for stent-assisted coil embolization of intracranial aneurysms. It is mechanically identical to the CREDO® Stent.

The six included case series and case reports, in which the NeuroSpeed® PTA Balloon Catheter was used together with the CREDO® Stent as well as the six publications on the use of the NeuroSpeed® PTA Balloon Catheter with the ACCLINO® flex Stent have quite similar retrospective study designs. All included publications were uncontrolled and had varying numbers of enrolled patients. Indications and location of stenoses are in line with the intended use and indication given by Acandis. One case series (Bhogal et al. 2022) described the use of the NeuroSpeed® PTA Balloon Catheter alone, in all other cases it was used together with a stent.

Table 4: Outcome parameters of pivotal clinical data (mRS = modified Rankin Scale, NIHSS = National Institutes of Health Stroke Scale, mENR = major early neurological recovery, sICH = symptomatic intracranial hemorrhage, ICS = intracranial atherosclerotic stenosis, eICS = elective intracranial stenting, FBTS = first balloon then stent, SAE = serious adverse event, n.a. = not applicable)

Author	Technical success	Pre-procedural stenosis	Post-procedural stenosis	Neurological outcome	Complications	Conclusion on safety and performance
Möhlenbruch et al. 2016	100 %	82.5 % (median)	10 %	mRS: Unchanged: n = 4 (2 x 1, 1 x 4, 1 x 3) significantly improved: n = 2 (2 to 1; 1 to 0)	None	FBTS bears the specific potential to reduce wire perforations, which so far have been linked to major procedure-related adverse events of endovascular ICS treatment.
Stracke et al. 2020b	--- mTICI ≥ 2b: 29.6 %	-	-	mENR: n = 19 mRS ≤ 2: n = 13 (of 32 as 18 are missing) NIHSS: Improved non-significantly from 12 to 8 (median)	No intervention-related SAEs sICH: 4 % 90-day mortality: 17.1 %	Intracranial bailout stenting with the ACCLINO (Flex) Stent and the NeuroSpeed Balloon Catheter after failed MT is a feasible and effective recanalization method for atherosclerotic stenosis-based Stroke that is especially associated with low rates of sICH.
Meyer et al. 2020b	100 %	-	-	mRS all unchanged (median mRS = 1)	No intervention-related SAEs Peri-procedural stroke: 6.5% Asymptomatic ICH: 5.2 % In-stent restenosis: 25 % Stroke recurrence: 1.3 % Stroke-related deaths: 2.6 %	Stenting for symptomatic intracranial stenosis with the ACCLINO (flex) / NeuroSpeed balloon catheter was safe and reinforced eICS as an endovascular therapy option for secondary stroke prevention.
Stracke et al. 2020a	--- mTICI ≥ 2b: 82.9 %	-	-	mRS 1 – 2: n = 15 mRS 3: n = 20 NIHSS improved from 13 to 6 (median)	sICH: 9.1 %	The use of the ACCLINO/ACCLINO flex stent (Acandis GmbH) was associated with a significantly lower rate of sICH. Use of rescue stent angioplasty can be considered for acute intracranial large vessel occlusion in cases after unsuccessful stent-retriever thrombectomy.

Author	Technical success	Pre-procedural stenosis	Post-procedural stenosis	Neurological outcome	Complications	Conclusion on safety and performance
Capirossi et al. 2022	Disappearance of stenotic diaphragm with a minimal residual stenosis	High-grade	Minimal	Not assessed	No complications	Endovascular treatment is an effective and safe method for eliminating pulsatile tinnitus in patients with severe intracranial carotid artery stenosis.
Borota et al. 2022	100 %	Not assessed	Reconstructed lumen of the but narrowed origins of superior cerebellar arteries	mRS 1 at discharge, NIHSS and mRS 0 after 11 months	Pneumonia, swallowing problems, tetraplegia	Despite a huge pons infarction and the two different interventions a few hours apart, the neurological outcome was surprisingly favorable in this patient.
Giang et al. 2022	No (first attempt with NeuroSpeed) 100 % with second intervention	Not assessed	Not assessed	After second intervention: mRS 1 3 months after discharge	After first intervention: Hemiplegia, increase in hypertense lesions in the left hemisphere, near occlusion in the left internal carotid artery Second intervention: none	With the first intervention using the NeuroSpeed PTA Balloon Catheter, the the stent could not reach the stenosis site due to the presence of a tortuous type III aortic arch in the left CCA. In a second approach, a transcervical approach instead of the transfemoral was used and succeeded. No conclusions on the safety and performance of the NeuroSpeed PTA Balloon Catheter were drawn.

Most of the publications evaluated the safety and performance of the procedure in general or the additionally used stents, Therefore, only limited information on NeuroSpeed® PTA Balloon Catheter-related endpoints alone could be extracted from these publications.

1.5.3.3 Summary and conclusion on safety and clinical performance

The purpose of PTA for atherosclerotic occlusion is to achieve long-term patency by mechanical dilatation. The studies applied recognized radiological endpoints (improved patency and perfusion) as well as patient-centered endpoints providing evidence on the clinical results (improved symptoms, recurrent symptoms, adverse neurological events). However, as the NeuroSpeed® PTA Balloon Catheter was mostly described together with the use of a stent, only indirect conclusions on its contribution to the technical and clinical success can be drawn. As the success rates in general were high, it can be concluded that the NeuroSpeed® PTA Balloon Catheter fulfilled its intended use. Additionally, complications related to the NeuroSpeed® PTA Balloon Catheter or the procedure of PTA were low, thus, it can be deemed safe in its intended use.

Chosen endpoints

The most important clinical endpoint to determine the performance of the NeuroSpeed® PTA Balloon Catheter with or without the CREDO® Stent (or the ACCLINO® (flex) Stent when used in stroke treatment) is the rate of vessel lumen patency as well as neurological outcome. In total, only two articles gave the stenosis grade before and after the procedure (Möhlenbruch et al. 2016; Buonomo et al. 2021), a third article described it in words (Capirossi et al. 2022). In all three cases, patency improved. One publication described the use of NeuroSpeed PTA Balloon Catheter alone. Here, the NeuroSpeed® PTA Balloon Catheter was applied for angioplasty of fish-mouthing of the p64MW HPC flow diverter (phenox GmbH, Bochum, Germany) after aneurysm occlusion (Bhogal et al. 2022).

Neurological outcome assessed by mRS was unchanged or even improved in most publications. Favorable functional outcome is defined as mRS ≤ 2.

1.5.3.4 Clinical data obtained by clinical trials or PMCF-measures

Acandis has been conducting the registry ASSISTENT (AcandiS Stenting of Intracranial STENosis – RegisTry) since July 2016. The study was interrupted and restarted. Recruitment is ongoing until March 2025.

1.5.3.5 Clinical data from medical device databases

BfArM (German Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) database of Field Corrective Actions): Latest search in April 2023: No entries concerning the NeuroSpeed® PTA Balloon Catheter.

MAUDE ("Manufacturer and User Facility Device Experience (MAUDE) Database, maintained by the United States' Food and Drug Administration), latest search in April 2023.
Some entries concerning the benchmark device Gateway PTA balloon catheter: The entries deal with risks and complications inherent to the risk profile of intracranial PTA balloon catheters and endovascular procedures. Hence, these risks are known to the trained and experienced physician who knows how to handle them.
Overall, these entries do not indicate high failure or incident rates of PTA balloon catheters which are comparable to the NeuroSpeed® PTA Balloon Catheter. Thus, there is no allusion to an unfavorable risk profile of such systems in routine clinical use.

1.5.4 An overall summary of the clinical performance and safety

The clinical literature reflecting the state-of-the-art in treatment of intracranial stenoses with intracranial neurovascular stents combined with intracranial PTA balloon catheters, including the use of the NeuroSpeed® PTA Balloon Catheter, together with the results from the searches in authority-maintained vigilance databases as well as the data collected from the PMCF study on the NeuroSpeed® PTA Balloon Catheter prove the clinical performance and safety of the NeuroSpeed® PTA Balloon Catheter. The reviewed studies provide sound evidence that by using these devices, a successful and safe treatment of intracranial stenoses is feasible. It could be shown that the combination of NeuroSpeed® PTA Balloon Catheter and CREDO® Stent/ACCLINO® (flex) Stent achieves technical and clinical success rates that are comparable to the state-of-the-art. Technical success could be reached in 92 % (ASSISTENT study) and 97 – 100 % (literature) of the patients respectively. Clinical success in terms of mRS 0 – 2 was reached in 58 % (ASSISTENT study) and 40 % (literature) of patients. The overall complication rate was 26.9 % (ASSISTENT study) of patients. From scientific literature this number cannot be directly derived as the complications are described not as depicted as in the study reports.

According to the clinical data presented in the scientific literature, the information gained from the ASSISTENT study and PMS as well as the risk analysis, it can be concluded that risks which may be associated with the intended use of the NeuroSpeed® PTA Balloon Catheter constitute acceptable risks when weighed against the benefits to the patient. Further, it can be concluded that for patients carefully selected for this treatment, undesirable side-effects constitute an acceptable risk when weighed against the performance intended by the clinician in charge. The main risks are described and documented in detail in the scientific literature, thus being known to trained professional user. Therefore, by complying with all warnings and precautions, the NeuroSpeed® PTA Balloon Catheter offers an acceptable benefit-risk profile and meets the requirement for an acceptability of side effects and acceptable benefit-risk profile.

Clinically relevant marketing claim in Acandis' brochure: Unique treatment concept – PTA and stenting without catheter exchange. This marketing claim is acceptable due to the delivery procedure, which allows subsequent stenting after balloon dilation.

In conclusion, the NeuroSpeed® PTA Balloon Catheter could be shown to be in compliance with the General Safety and Performance Requirements specified by the Medical Device Regulation (MDR) EU 2017/745.

1.5.5 Ongoing or planned post-market clinical follow-up

Acandis has been conducting the registry ASSISTENT (AcandiS Stenting of Intracranial STENosis – RegisTry) since July 2016. The study was interrupted and restarted. Recruitment is ongoing until March 2025. An interim PMCF study report after enrollment of 26 patients is available: The technical success with the CREDO® Stent and NeuroSpeed® PTA Balloon Catheter was high (92 %), the rate of immediate peri-procedural complications as well as clinical outcome events after 30 days were low. Although this interim analysis only included 26 patients in the second study period, the interim results are comparable to previous studies on intracranial stenting.
A further PMCF study "RECHRUT" is ongoing with the CREDO® heal Stent. Recruitment has started in March 2023. Enrollment duration is planned until March 2026.

1.6 Possible diagnostic or therapeutic alternatives

There are treatment alternatives to intracranial stenting. These include medical management, surgery, mechanical thrombectomy and percutaneous intraluminal angioplasty without stenting. For each patient it should be evaluated individually, which treatment option is the most promising for good neurological outcome. Concluding from the scientific literature, surgery is associated with the least favorable neurologic outcome, whereas mechanical thrombectomy is a standard treatment of acute ischemic stroke caused by large vessel occlusion. PTA is widely applied in arterial stenosis treatment. Balloon angioplasty and/or stenting was feasible in acute large vessel occlusions, resulting in favorable angiographic and clinical outcomes with an acceptable safety profile widely (4 – 40 %) within 30 days of treatment. However, restenosis is also seen in 24 – 50 % of these patients.

1.7 Suggested profile and training for users

Physicians who have the necessary background knowledge and experience in interventional neuroradiology and stent-assisted percutaneous transluminal angioplasty (PTA).

1.8 Reference to harmonised standards and common specifications applied

Standard	Title	Revision
EN 556-1	Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices	2001 +AC:2006
EN 868-2	Packaging for terminally sterilised medical devices - Part 2: Sterilization wrap – Requirements and test methods	2017
EN ISO 10555-4	Sterile, single-use intravascular catheters. Balloon dilatation catheters (ISO 10555-4:2013)	2013
EN ISO 10555-1	Sterile, single-use intravascular catheters - Part 1: General requirements (ISO 10555-1:2013 + Amd 1:2017)	2013+ A1:2017
EN ISO 10993-23	Biological evaluation of medical devices - Part 23: Tests for irritation (ISO 10993-23:2021)	2021
EN ISO 10993-18	Biological evaluation of medical devices - Part 18: Chemical characterization of medical device materials within a risk management process (ISO 10993-18:2020)	2020
EN ISO 10993-17	Biological evaluation of medical devices - Part 17: Establishment of allowable limits for leachable substances (ISO 10993-17:2002)	2009
EN ISO 10993-12	Biological evaluation of medical devices - Part 12: Sample preparation and reference materials (ISO 10993-12:2021)	2021
EN ISO 10993-11	Biological evaluation of medical devices - Part 11: Tests for systemic toxicity (ISO 10993-11:2017)	2018
EN ISO 10993-7	Biological evaluation of medical devices - Part 7: Ethylene oxide sterilization residuals (ISO 10993-7:2008 + Cor 1:2009 + Amd 1:2019)	2008 + AC:2009 +A1:2022
EN ISO 10993-5	Biological evaluation of medical devices- Part 5: Tests for in vitro cytotoxicity (ISO 10993-5:2009)	2009
EN ISO 10993-4	Biological evaluation of medical devices - Part 4: Selection of tests for interactions with blood (ISO 10993-4:2017)	2017
EN ISO 10993-3	Biological evaluation of medical devices - Part 3: Tests for genotoxi-city, carcinogenicity and reproductive toxicity (ISO 10993-3:2014)	2014
EN ISO 10993-2	Biological evaluation of medical devices - Part 2: Animal welfare requirements (ISO 10993-2:2022)	2022
EN ISO 10993-1	Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process (ISO 10993-1:2018, including corrected version 2018-10)	2020
EN ISO 11135	Sterilization of health care products – Ethylene oxide - Requirements for the development, validation and routine control of a sterilization process for medical devices (ISO 11135:2014+Amd.1:2018)	2014 +A1:2019
EN ISO 11138-2	Sterilization of health care products - Biological indicators - Part 2: Biological indicators for ethylene oxide sterilization processes (ISO 11138-2:2017)	2017
EN ISO 11138-1	Sterilization of health care products - Biological indicators - Part 1: General requirements (ISO 11138-1:2017)	2017
EN ISO 11139	Sterilization of health care products – Vocabulary of terms used in sterilization and related equipment and process standards (ISO 11139:2018)	2018
EN ISO 1 11607-2	Packaging for terminally sterilised medical devices - Part 2: Validation requirements for forming, sealing and assembly processes (ISO 11607-2:2019)	2020 +A11:2022
EN ISO 11607-1	Packaging for terminally sterilised medical devices - Part 1: Requirements for materials, sterile barrier systems and packaging systems (ISO 11607-1:2019)	2020 +A11:2022
EN ISO 11737-1	Sterilization of health care products - Microbiological methods - Part 1: Determination of a population of microorganisms on products (ISO 11737-1:2018 + Amd 1:2021)	2018 + A1:2021
EN ISO 13485	Medical devices - Quality management systems - Requirements for regulatory purposes (ISO 13485:2016)	2016 +AC:2018 +A11:2021
EN ISO 14644-5	Cleanroom and associated controlled environments - Part 5: Operations (ISO 14644-5:2004)	2004
EN ISO	Cleanroom and associated controlled environments - Part 4: Design, construction and start-up (ISO 14644-4:2001)	2001

Standard	Title	Revision
14644-4		
EN ISO 14644-3	Cleanrooms and associated controlled environments - Part 3: Test methods (ISO 14644-3:2019)	2019
EN ISO 14644-2	Cleanrooms and associated controlled environments - Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration (ISO 14644-2:2015)	2015
EN ISO 14644-1	Cleanrooms and associated controlled environments - Part 1: Classification of air cleanliness by particle concentration (ISO 14644-1:2015)	2015
EN ISO 14698-2	Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data TECHNICAL CORRIGENDUM 1	2003/ Cor. 1:2004
EN ISO 14698-1	Cleanroom and associated controlled environments – Biocontamination control - Part 1: General principles and methods (ISO 14698-1:2003)	2003
EN ISO 14971	Medical devices. Application of risk management to medical devices (ISO 14971:2019)	2019+ A11:2021
EN ISO 15223-1	Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements (ISO 15223-1:2021)	2021
EN 17141	Cleanrooms and associated controlled environments - Biocontamination control	2020
EN ISO 20417	Medical devices - Information to be supplied by the manufacturer (ISO 20417:2021)	2021
EN 62366-1	Medical devices - Part 1: Application of usability engineering to medical devices (IEC 62366-1:2015 + COR1:2016 + A1:2020)	2015+AC:2015 + A1:2020
EN ISO 80369-7	Small-bore connectors for liquids and gases in healthcare applications - Part 7: Connectors for intravascular or hypodermic applications (ISO 80369-7:2021)	2021

2 Information for the patient

This part of the SSCP is not deemed necessary for the NeuroSpeed® PTA Ballon Catheter.

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