ENGINEERING STROKE SOLUTIONS

# Summary of Safety and Clinical Performance:

# CREDO® Stent
# Acandis GmbH

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

Identifier: 2700

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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 CREDO® Stent.

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 CREDO® Stent nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.

The following information is intended for users/healthcare professionals.
In addition to this information, there is a summary intended for patients (chapter 2).

## 1.1 Device identification and general information

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| **Device trade name(s)** | CREDO® Stent<br>Article no.<br>01-000930 – 01-000933<br>01-000935 – 01-000938<br>01-000940 – 01-000943<br>01-000945 – 01-000948<br>01-000950 – 01-000953 |
| **Manufacturer's name and address** | Acandis GmbH,<br>Theodor-Fahrner-Straße 6, 75177 Pforzheim, Germany |
| **Manufacturer's single registration number (SRN)** | DE-MF-000006259 |
| **Basic UDI-DI** | 426065033CREDO3K |
| **Medical device nomenclature** | UMDNS: 17-461 (vascular stent)<br>GMDN: 46352 (bare-metal intracranial vascular stent)<br>EMDN: P0799 (vascular and cardiac prostheses – other) |
| **Class of device** | Class III medical device, as defined in Medical Device Regulation (MDR) EU 2017/745, Annex VIII, rule 8, bullet point 2 |
| **Year of first CE certificate** | 2015 |
| **Authorized representative** | not applicable |
| **Notified body** | DQS Medizinprodukte GmbH (Notified body number: 0297). |

### 1.2 Intended use of the device

<table>
<tr><td>Intended purpose</td><td colspan="2">The CREDO® Stent is intended for the treatment of intracranial stenosis by keeping the blood vessel open after necessary pretreatment has been performed.</td></tr>
<tr><td rowspan="2">Indication(s)</td><td colspan="2">The CREDO® Stent is indicated, together with the NeuroSpeed® PTA Balloon Catheter, for the dilatation of the diameter of intracranial arteries (for example ICA, MCA, VA/V4, BA) which are accessible to and suitable for the system (stent with PTA balloon catheter).</td></tr>
<tr><td>…in patients<br>- with stenosis (high-grade intra-cranial stenoses > 70 %) probably resulting from arteriosclerosis (as established clinically, from case history or from laboratory tests), where there is clear circulatory disturbance (hemodynamic infarction pattern and evidence of limited collateral vessels) despite intensive drug therapy,<br>- who have become symptomatic again despite antiplatelet therapy following at least two events (stroke) (treatment-refractory),<br>- who are over 18 years of age,<br>- in whom the most recent stroke occurred at least 7 days previously, with a diagnosed impairment after the stroke of 3 or less on the modified Rankin scale (mRS) at the time of treatment.</td><td>or<br>…in patients<br>- with evidence of an intracranial large vessel occlusion (LVO),<br>- who are over 18 years of age,<br>- with an acute persistent vessel occlusion resulting from a high-grade intracranial stenosis, for which alternative treatment options are not possible or have failed,<br>- with a suspected underlying stenosis of the occluded artery, which is amenable to PTA and stenting in the opinion of the treating physician,<br>- with a small to medium infarct core prior to commencement of thrombectomy (CT score ASPECTS 6 – 10, DWI lesion < 70 ml)</td></tr>
<tr><td rowspan="2">Targeted population(s)</td><td colspan="2">Intended user:<br>The CREDO® Stent and the NeuroSpeed® PTA Balloon Catheter should be applied only by physicians who have the necessary background knowledge and experience in the field of interventional neuroradiology and stent-assisted percutaneous transluminal angioplasty (PTA).</td></tr>
<tr><td colspan="2">Patient target group:<br>No special patient populations defined but patients with contraindications are to be excluded.</td></tr>
<tr><td>Contraindications and/or limitations</td><td colspan="2">- Patients in whom the diameter of the healthy vessel proximally and distally to the stenosis does not permit safe treatment with the NeuroSpeed® PTA Balloon Catheter (see instruction for use of the NeuroSpeed® PTA Balloon Catheter).<br>- Patients in whom the diameter of the healthy vessel proximally and distally to the stenosis lies outside the indicated range of the CREDO® Stent. For the corresponding specifications, refer to the label.<br>- Patients in whom the diameter of the target area after pre-dilatation lies outside the indicated range of the CREDO® Stent. For the corresponding specifications, refer to the label.</td></tr>
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| | |
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| | - Patients in whom antiplatelet and/or anticoagulant therapy is contra-indicated.<br>- Patients with highly calcified lesions which could prevent access or safe introduction of the stent.<br>- Patients who present in the angiography with anatomical conditions unsuitable for endovascular treatment.<br>- Patients who are hypersensitive to nickel-titanium.<br><br>No limitations are mentioned in the IFU. |

## 1.3 Device description

The CREDO® Stent is a self-expanding, laser-cut stent made of nitinol (a nickel-titanium alloy). The stent has a closed cell design and three radiopaque platinum/iridium markers each at the proximal and distal ends. The stent is preloaded on a transport wire in an introducer. The tip of the transport wire is J-shaped. The sizes are specified on the packaging label.
In order to make fluoroscopic placement easier, there are likewise three X-ray markers on the transport wire. The distal marker shows the tip of the transport wire, the central marker identifies the centre of the stent and the proximal marker shows the point up to which the stent can be repositioned. The CREDO® Stent is implanted for life.

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| **Sizes** | Ø 3.0 / 3.5 / 4.0 / 4.5 / 5.0 mm, lengths: 15 / 20 / 25 / 30 mm |
| **Sterility** | Yes, for single-use |
| **Generic device group** | Intracranial neurovascular stent, self-expandable |
| **MR conditional:** | up to 3Tesla |
| **Foreshortening** | < 30 % |
| **Stent surface area** | ≤ 11 % |

Stent placement after Balloon PTA is possible without changing the catheter.
Patented asymmetric closed cell design of the CREDO Stent leads to highest flexibility in its class of laser-cut stents. The stent features excellent vessel wall apposition and conformability even in challenging anatomies.
Extra flat stent structure and perfectly electropolished surface enable smooth delivery. Stent structure ensures high permeability in the vessel lumen and leads to a low thrombogenicity.
Easy and clear radiopaque marker concept and good visibility ensure accurate positioning as well as optimal control during procedure. The stent is repositionable up to 90 % of its length.
The preloaded stent is transferred with the help of the introducer into the balloon catheter and is guided to the target zone with the corresponding transport wire. The implant is deployed by pulling the balloon catheter backwards while simultaneously holding the transport wire at fixed position. The stent expands by an elastic restoring force once released from the balloon

catheter. A repositioning of the stent is possible until the point of no return is reached. The stent is repositioned by pushing the balloon catheter carefully over the partially expanded stent. The implant covers the stenotic lesion maintaining blood flow to distal intracranial blood vessels after necessary pretreatment has been performed.

### 1.3.1 Previous generations

The first generation of the CREDO® Stent has been on the market since November 2015, the second generation since September 2018, the third generation (range extension) since January 2020, and the fourth generation (range extension and extension of indication) since January 2021.

### 1.3.2 Accessories

Transport wire guidance 2F.

### 1.3.3 Combination with other devices

The CREDO® Stent is intended for use in combination with the NeuroSpeed® PTA Balloon Catheter. The NeuroSpeed® PTA Balloon Catheter is the only catheter which was tested for compatibility with the CREDO® 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. (Pseudo)aneurysm, (Intracerebral) haemorrhage, Embolism (air, foreign body, plaque or thrombus), Fever, Vessel dissection, Vessel perforation, Vessel rupture, Vessel stenosis, Vessel trauma, (Abrupt) vessel occlusion or thrombosis, Cerebral oedema, Hyperperfusion syndrome, Infection, (Cerebral) ischemia/infarction, Secondary haemorrhage, Reactions due to radiation exposure, Subarachnoid haemorrhage, 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 stent delivery/implantation (e.g. Stent breakage, Stent folding, Incorrect stent placement, Stent cannot be released, Stent cannot be drawn

back into catheter, Stent bending, Stent does not detach from transport wire, Stent migration, Insufficient opening, Delayed treatment, Target area inaccessible or cannot be accessed safely, Additional stenting required).

- Other complications in connection with the stent (e.g. Allergic reactions to the stent material, In-stent stenosis, Perforator infarction, Reoperation, (Re)stenosis, Stent occlusion/thrombosis, Occlusion of perforators or branching vessels).
- Neurological deficits (e.g. Dysphasia, Hemiparesis, Hemiplegia, Impaired vision, Oculomotor paresis, Speech disorders).
- Death.

In the scientific literature, the most commonly reported complication is intracranial hemorrhage. Symptomatic intracranial hemorrhage occurred in 4 % (Stracke et al. 2020b) and 9.1 % (Stracke et al. 2020a), asymptomatic intracranial hemorrhage in 5.2 % (Meyer et al. 2020b). One publication (Meyer et al. 2020b) 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) and in another one, none were described (Gupta et al. 2023). 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 hemorrhage. 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 hemorrhage 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 hemorrhage 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. In their study, Forbrig et al. observed a mortality rate of 21 % (Forbrig et al. 2019). The mortality in the stenting group was 15 %. This was much lower than in the non-stenting group (50 %) (Pérez-García et al. 2020).

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. 2021b).

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 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 (mean: 64.8 ± 14.9 years, Mohammaden et al. 2022; 61.8 ± 13 years, Pérez-García et al. 2020; 67 years, Forbrig et al. 2019; 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 CREDO® Stent and the NeuroSpeed® PTA Balloon Catheter should be applied only by physicians who have the necessary background knowledge and experience in the field of interventional neuroradiology and stent-assisted percutaneous transluminal angioplasty (PTA).
- Before use, the product needs to be carefully checked to ensure there is no transportation damage. Under no circumstances should damaged or kinked components be used.
- Because application of the PTA balloon catheter involves the risk of subacute thrombosis, vascular complications and/or haemorrhages it is necessary to select patients with care.
- On no account whatsoever should you continue advancing the stent and the PTA balloon catheter if you encounter resistance without being aware of the cause. If you advance the stent and the PTA balloon catheter despite resistance, you could damage the stent and/or the PTA balloon catheter or perforate the vessel.
- The stent may be shorter after deployment.
- As the implantation of stents involves the risk of restenosis, repeat dilatation of the vessel section containing the stent may become necessary under certain circumstances. There are currently no findings on the risks and the long-term clinical outcome of repeat dilatation of endothelialised stents.

- Treatment of stenosis in arteries or areas of arteries with perforating branches (e.g. basilar artery) generally has an increased risk of complications.
- No specific patient populations have been defined but patients with contraindications are to be excluded.
- 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. Reusing, reprocessing or resterilisation may compromise the 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 crossinfection, 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 performance of a responder test is recommended to reduce the risk of complications. For this purpose, the efficacy of the antiplatelet agent is tested prior to application of the product.
- In order to minimise potential complications during and after the intervention, attention should be paid to careful medication treatment in accordance with the current guidelines from the medical societies (antiplatelet agents and anticoagulants prior to treatment and anticoagulants during the intervention). The administration of unsuitable antiplatelet agents and anticoagulants may lead to a stent thrombosis.
- The medication is an important part of the treatment. Patients must be advised to take medication regularly and informed of the potential risks of non-compliance.
- Guide wires or other devices must subsequently be passed extremely carefully through the stent once it has been implanted to minimise the potential risk of dislocating it.

### 1.4.3 Other relevant aspects of safety

There were no recalls, FSNs or FSCAs since market launch. The complaint rate is 0.25 % and the incident rate is 0.01 % from November 2019 to October 2023. A single CAPA was opened

regarding a mislabeling error of a guide wire component, measures to reduce the risk of mislabeling will be implemented. The medical benefit continues to outweigh the residual risk.
There were no relevant hits on unduly or unknown risks of the CREDO Stent in the databases of competent authorities.

## 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. Clinical data on the ACCLINO (flex) Stent by Acandis are described in chapter 1.5.3.2.

### 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 on the initial indication of intracranial stenting in non-acute ischemic strokes.
For the enhancement of the indication of acute strokes (stroke occurred within at least seven days previously), a clinical investigation was conducted between May 2019 and September 2021). The trial was terminated early, as enough clinical data were published in the meantime to receive the CE mark for the acute indication. The results are summarized in the following:

*Primary endpoints:*
Technical success defined as successful recanalization of the occluded vessel (TICI 2b – 3) at the end of the procedure was achieved in 88.9 % (65.3 % – 98.6 %). Good clinical outcome (mRS 0 – 2) at 90 (± 10) days after stroke was seen in 47.1% (23.0 % – 72.2 %) of patients. One patient was lost to follow-up for the clinical efficacy endpoint. 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).

*Secondary endpoints:*
There was no categorical shift in mRS after 90 (± 10) days and no frequency of residual stenosis > 50 %. 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 %.

### 1.5.3 Summary of clinical data from other sources

#### 1.5.3.1 Clinical data in the literature on the CREDO® Stent

Table 1: Study details and locations of the stenosis (ICS = intracranial atherosclerotic stenosis, TIA = transient ischemic stroke, ICA = intracranial atherosclerosis, VA = vertebral artery, BA = basilar artery, V4 = visual area 4, M1/M2 = segments in the middle cerebral artery, MCA = middle cerebral artery, HRF = high radial force).

| Author | Study design | # of patients | Used devices | Indications | Location of stenosis |
|---|---|---|---|---|---|
| Diana et al. 2021a | Case series | 10 | CREDO<br>2x 3x 15 mm / 1x 4 x 15 mm<br>1x 3 x 20 mm<br>Residual stents not named | Rescue stenting in patients with acute ischemic stroke and one case of stenting as first-line therapy. | MCA (n = 6)<br>Vertebra-basilar (n = 4) |
| Diana et al. 2021b | Case report | 1 | CREDO 4 x 15 mm<br><br>with NeuroSpeed<br>2.5 x 8 mm | Intracranial angioplasty and stenting in patients with high ischemic stroke risk. | ICA siphon |
| Cohen et al. 2022 | Case report | 1 | CREDO 3.0 x 20 mm<br><br>with first pITA PTA balloon catheter (phenox), then Excelsior XT-17 (Stryker) microcatheter for stent delivery | Severe stenosis | Distal M1 segment of the left MCA |
| Papa et al. 2020 | Case report (Conference abstract) | 3 | Neuroform (n = 1)<br>CREDO Stent (n = 2)<br><br>with NeuroSpeed PTA Balloon Catheter | Recurrent TIA or stroke after failure of best medical treatment | Not mentioned. |

| Author | Study design | # of patients | Used devices | Indications | Location of stenosis |
|---|---|---|---|---|---|
| Gupta et al. 2023 | Case report | 1 | AXS infinity LS (Stryker Neurovascular, Ireland) 0.014′ Traxcess microwire (Microvention Inc, Tustin, USA), 0.017′ Echelon microcatheter (Microtherapeutics.inc. Ev3 Neurovascular, USA), 0.038 DAC (Stryker Neurovascular USA) 5F Navien (Microtherapeutics.inc. Ev3 USA), microcatheter (0.017′) and microwire (Traxcess 0.014′) balloon angioplasty with 1.5 mm × 15 (Maverick, Boston Scientific) and 2.5 mm× 15 (Trek,Abbott costa rica) coronary balloon. CREDO 4 × 20 mm stent (Acandis GmbH., Pforzheim Germany) | Recurrent posterior circulation symptoms | Basilar artery |

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

| Author | Technical success | Neurological outcome | Complications | Conclusion on safety and performance |
|---|---|---|---|---|
| Diana et al. 2021a | Optimal: 75 %<br>Suboptimal: 25 % | Of 4 CREDO procedures reported:<br>mRS ≤ 2: n = 2 | Of 4 CREDO procedures reported:<br>Watershed SAH: 100 %<br>ICH: 25 %<br>Mortality: 25 % | Watershed ICH may occur after stenting of the MCA. It might be linked with biological and hemodynamic alterations of the cerebral autoregulation mechanism and might precede the hyper-perfusion syndrome. |
| Diana et al. 2021b | 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. |
| Capirossi et al. 2022 | Disappearance of stenotic diaphragm with a minimal residual stenosis | Not assessed | No complications | Endovascular treatment is an effective and safe method for eliminating pulsatile tinnitus in patients with severe intracranial carotid artery stenosis. |
| Cohen et al. 2022 | The stent fully expanded and corrected the intra-luminal filling defects, adequate revascularization of the MCA. | Not assessed | None | After stenting, the patient had an uncomplicated subsequent hospital course with a remarkably rapid and complete reversal of his symptoms. |
| Papa et al. 2020 | Successful in all patients | Not assessed | None | Clinical and angiographic results were encouraging. More data are mandatory to confirm the clinical benefit of endovascular treatment of intracranial stenosis. |
| Gupta et al. 2023 | Successful deployment | Not assessed | None | The stent was well apposed with minimal residual stenosis |

### 1.5.3.2 Clinical data in the literature on the mechanically identical ACCLINO® (flex) Stent

The ACCLINO® flex Stent obtained CE marking in February 2014 and has been developed for stent-assisted coil embolization of intracranial aneurysms. It is technically identical to the CREDO® Stent and thus frequently used off-label in the (bail-out) treatment of stroke.

Table 3: Study details and locations of the stenosis (ICS = intracranial atherosclerotic stenosis, TIA = transient ischemic stroke, ICA = intracranial atherosclerosis, VA = vertebral artery, BA = basilar artery, V4 = visual area 4, M1/M2 = segments in the middle cerebral artery, MCA = middle cerebral artery, HRF = high radial force).

| Author | Study design | # of patients | Used devices | Indications | Location of stenosis |
|---|---|---|---|---|---|
| Möhlenbruch et al. 2016 | Case series: Retrospective review of prospectively collected database | 6 | ACCLINO flex Stent:<br>2x 3.5 x 15 mm / 1x 3.5 x 20 mm<br>1x 4.5 x 15 mm / 2x 4.5 x 20 mm<br><br>with NeuroSpeed | 1) failure of dual antiplatelet therapy defined as recurrent TIA or ischemic stroke<br>2) presence of ICS of ≥ 70 %<br>3) endovascular accessibility of the target lesion as judged by CT angiography or MRI angiography | V4 (n = 3)<br>M1 (n = 2)<br>supraclinoid portion of the ICA (n = 1) |
| Stracke et al. 2020a | Case series: retrospective review | 50 | ACCLINO (flex)<br><br>with NeuroSpeed | Bailout stenting for acute ischemic stroke after failed thrombectomy | M1 (n = 17)<br>M2 (n = 1)<br>VA (n = 10)<br>BA (n = 14) |
| Meyer et al. 2020b | Case series: multi-center cohort study | 76 | ACCLINO (flex) Stent<br><br>with<br>NeuroSpeed: n = 58<br>Microcatheters n = 18 | Secondary stroke prevention in patients with symptomatic intracranial stenosis due to<br>1) Recurrent stroke<br>2) TIA | Terminal internal carotid artery (n = 21)<br>M1 (n = 17)<br>M2 (n = 2)<br>Anterior cerebral artery (n = 2)<br>V4 (n = 23)<br>BA (n = 11) |
| Forbrig et al. 2019 | Clinical study: retrospective analysis | 34 | ACCLINO (n = 6)<br>Enterprise (n = 15)<br>Solitaire (n = 8)<br>Wingspan (n = 6)<br>Coroflex Blue Ultra (n = 1)<br>Leo (n = 1) | Rescue stent angioplasty for acute large vessel occlusion:<br>1) Immediate reocclusion<br>2) Persistent high-grade stenosis | BA (n = 12)<br>M1 (n = 11)<br>Distal ICA (n = 4)<br>Petrous ICA (n = 1)<br>M2 (n = 2)<br>V4 (n = 4) |

| Author | Study design | # of patients | Used devices | Indications | Location of stenosis |
|---|---|---|---|---|---|
| Pérez-García et al. 2020 | Clinical study: retrospective analysis of a prospective cohort | 60 | ACCLINO (n = 1)<br>Wingspan (n = 9)<br>Neuroform (n = 6)<br>Solitaire (n = 3)<br>Enterprise (n = 3)<br>Pharos (n = 2)<br>Neuroform Atlas (n = 2) | Rescue stenting after failed mechanical thrombectomy (20 patients) of patients with ischemic stroke. | Stenting group:<br>Distal ICA (n = 9)<br>MCA (n = 11)<br><br>Non-stenting group:<br>Distal ICA (n = 12)<br>MCA (n = 28) |
| Stracke et al. 2020a | Clinical study: retrospective analysis | 61 | ACCLINO (flex)<br><br>with<br>NeuroSpeed<br>Microcatheters | Bailout stenting for acute ischemic stroke after failed thrombectomy | ICA<br>M1<br>M2<br>VA<br>BA<br>(Numbers not separated for different stent types used) |
| Capirossi et al. 2022 | Case report | 1 | ACCLINO flex HRF 5.0 x 25 mm<br><br>with NeuroSpeed 4.0 x 8 mm | Symptomatic right carotid syphon stenosis; one month earlier there was a minor stroke with left hemiparesis. | Right carotid syphon |

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

| Author | Technical success | Neurological outcome | Complications | Conclusion on safety and performance |
|---|---|---|---|---|
| Möhlenbruch et al. 2016 | 100 % | mRS: Unchanged: n = 4 (2x 1, 1x 4, 1x 3)<br>significantly improved: n = 2 (2 to 1; 1 to 0) | None<br>Post-procedural stenosis: 10 % | 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. 2020a | -<br><br>mTICI ≥ 2b: 29.6 % | mENR: n = 19<br>mRS ≤ 2:<br>n = 13 (of 32 as 18 are missing)<br>NIHSS: Improved non-sig-nificantly from 12 to 8 (median) | No intervention-related SAEs<br>sICH: 4 %<br>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. |

| Author | Technical success | Neurological outcome | Complications | Conclusion on safety and performance |
|---|---|---|---|---|
| Meyer et al. 2020b | 100 % | mRS<br>all unchanged<br>(median mRS = 1) | No intervention-related SAEs<br>Peri-procedural stroke: 6.5 %<br>Asymptomatic ICH: 5.2 %<br>In-stent restenosis: 25 %<br>Stroke recurrence: 1.7 %<br>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. |
| Forbrig et al. 2019 | 97 %<br><br>mTICI ≥ 2b:<br>76 % | NIHSS:<br>improved substantially in 47 %<br><br>mRS (0 – 2):<br>n = 10 | sICH: 12 %<br>stent-occlusion: 18 %<br>asymptomatic stent occlusion: 9 %<br>mortality: 21 % | With one ACCLINO, stent placement was not successful. Rescue stent angioplasty is the only chance to permanently restore blood flow in patients with underlying vessel pathology and immediate reocclusion or high-grade stenosis after initially successful stent retriever thrombectomy. Rescue stenting was feasible showed good recanalization results. |
| Pérez-García et al. 2020 | Stenting group:<br><br>mTICI ≥ 2b:<br>70 % | Stenting group:<br>mRS ≤ 2): n = 9<br><br>NIHSS improvement from 18 ± 10 to 9 ± 14<br><br>Non-stenting group:<br>mRS ≤ 2): n = 1<br><br>NIHSS change from 20 ± 8.5 to 23 ± 6-75 | Stenting group:<br>sICH: 10 %<br>mortality: 15 %<br><br>Non-stenting group:<br>sICH: 2.5 %<br>mortality: 50 % | Remaining occlusion occurred in four patients (two Wingspan, one Pharos, one Solitaire).<br><br>Placement of an intracranial stent for rescue therapy after failed mechanical thrombectomy showed better clinical outcome without significant increase of hemorrhagic complications than non-stenting. |
| Stracke et al. 2020a | -<br><br>mTICI ≥ 2b:<br>82.9 % | mRS 1 – 2: n = 15<br><br>mRS 3: n = 20<br><br>NIHSS improved from 13 to 6 (median) | sICH: 3.3 % | 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. |
| Capirossi et al. 2022 | Disappearance of stenotic diaphragm with a minimal residual stenosis | Not assessed | No complications | Endovascular treatment is an effective and safe method for eliminating pulsatile tinnitus in patients with severe intracranial carotid artery stenosis. |

#### 1.5.3.3 Clinical data obtained by clinical trials or PMCF-measures

In addition to the ACUTE trial (see chapter 1.5.2), Acandis has been conducting the registry ASSISTENT (AcandiS Stenting of Intracranial STENosis – RegisTry) since July 2016. The study was interrupted. Recruitment is ongoing until March 2025.

#### 1.5.3.4 Clinical data from medical device databases

The medical device databases “Manufacturer and User Facility Device Experience (MAUDE) Database” maintained by the United States’ Food and Drug Administration as well as the German Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) database of Field Corrective Actions were searched for clinical data on the CREDO® Stent during the preparation of the clinical evaluation report. The searches for the BfArM were conducted on March 05th, 2024 and the searches for the MAUDE were conducted on March 11th, 2024. The time frame was not limited for the BfArM search. The time frame for the MAUDE search comprised April 1st, 2023 to February 29th, 2024.

The BfArM database search revealed no new entries regarding recalls and incidents. There was no medical risk for patients or increased risk of injury to users.
The MAUDE database search revealed entries for injuries and malfunctions. The entries deal with risks and complications inherent to the risk profile of intracranial stenting and endovascular procedures as well as off-label use of the Wingspan stent. 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 neurovascular stents which are comparable to the CREDO® Stent. 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 purpose of intracranial stenting is to increase the vessel diameter of intracranial arteries. 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). As the success rates in general were high, it can be concluded that the CREDO® Stent fulfilled its intended use. Additionally, complications related to the CREDO® Stent or the procedure of intracranial stenting were mostly low, thus, it can be deemed safe in its intended use.

*Chosen endpoints*

The most important clinical endpoint to determine the performance of the CREDO® (or the ACCLINO® (flex) Stent when used in stroke treatment) is the rate of vessel lumen patency as well as neurological outcome.

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

### 1.5.4.1 Safety

Within the evaluated body of literature stating the use of the CREDO Stent and ACCLINO (flex) Stent in a total of 216 patients, the following complications and respective occurrence rates were reported (Table 5).

Table 5: Quantification of the occurrence rates of potential risks, complications and hazards from the SOTA and comparison with the occurrence rates reported for the DUE and the predecessor device.

| **Safety parameter (complication)** | **Occurrence rate described in the SOTA** | **Occurrence rate reported for the DUE** |
|---|---|---|
| SICH | 0 – 15 % (Hedayat et al. 2019; Meyer et al. 2020b) | 4 % (Stracke et al. 2020b)<br>3.3 % (Stracke et al. 2020a)<br>12.1 % (Forbrig et al. 2019)<br>10 % (Pérez-García et al. 2020)<br>7.7 % ASSISTENT<br>27.8 % ACUTE |
| Asymptomatic intracranial hemorrhage | 5.2 % (Meyer et al. 2020b) | 5.2 % (Meyer et al. 2020b)<br>7.7 % ASSISTENT |
| In-stent restenosis | 24 – 50 % (Gruber et al. 2021) | 25 % (Meyer et al. 2020b)<br>10.5 % (stent thrombosis) ASSISTENT |
| Stroke recurrence | 5 – 38.2 % (van den Wijngaard et al. 2016; Feng et al. 2017; Gruber et al. 2021) | 6.5 % (peri-procedural), 1.7 % (recurrent) (Meyer et al. 2020b)<br>3.9 % (non-disabling in the region of the target vessel),<br>7.7 % (disabling in the region of the target vessel),<br>3.9 % (disabling outside the region of the target vessel) ASSISTENT |
| Mortality | 3 – 40 % (Feng et al. 2017; Gruber et al. 2021) | 5.2 % (Meyer et al. 2020b)<br>21 % (Forbrig et al. 2019)<br>15 % (Pérez-García et al. 2020)<br>18.5 % (Stracke et al. 2020a)<br>17.1 % (Stracke et al. 2020b)<br>25 % (Diana et al. 2021a)<br>7.7 % ASSISTENT<br>33 % ACUTE |
| TIA | 10 % (Feng et al. 2017) | 3.9 % ASSISTENT |
| PH-2 | 3.33 % (Pérez-García et al. 2020) | 5.6 % ACUTE |
| Ischemic events | 8 – 14.7 % (Feng et al. 2017; Gruber et al. 2021) | 0 ischemic strokes in ASSISTENT<br>0 ischemic strokes in ACUTE |

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 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 (mean: 64.8 ± 14.9 years, Mohammaden et al. 2022; 61.8 ± 16.5 years, Pérez-García et al. 2020; 67 years, (Forbrig et al. 2019); median: 67 (59 – 75) years; Stracke et al. 2020a; 71 (61 – 79) years, Stracke et al. 2020b).

The overall complication rate was 27.8 % (ACUTE trial) and 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.

### 1.5.4.2 Technical and clinical success

Performance of the CREDO® Stent includes proper increase the vessel diameter of intracranial arteries (technical success) as well as improvement of recanalization, technical success without complications, stroke or death, neurological outcome (clinical outcome). In literature, they are assessed using the mTICI, mRS and NIHSS scores and by description of stroke and mortality rates. Details are depicted in Table 6.

Table 6: Technical and clinical success from the SOTA and comparison with the rates described for the DUE and its predecessor device

| Performance parameter | Occurrence rate described in the SOTA | Occurrence rate reported for the DUE |
|---|---|---|
| Technical success | 87.8 % (Peng et al. 2020) – 88 % (Li et al. 2020) | 100 % (Möhlenbruch et al. 2016)<br>100 % (Meyer et al. 2020b)<br>97 % (Forbrig et al. 2019)<br>75 % (Diana et al. 2021a)<br>100 % (Cohen et al. 2022)<br>100 % (Papa et al. 2020)<br>92 % ASSISTENT |
| Clinical success mTICI ≥ 2b | 90 % (Meyer et al. 2020a) | 29.6 % (Stracke et al. 2020b)<br>76 % (Forbrig et al. 2019)<br>70 % (Pérez-García et al. 2020)<br>82.9 % (Stracke et al. 2020a)<br>88.9 % ACUTE |
| Clinical success mRS ≤ 2 | 36.4 % (Peng et al. 2020) - 74.1 % (Meyer et al. 2020a) | 66.7 % (Möhlenbruch et al. 2016)<br>26 % (Stracke et al. 2020b)<br>100 % (median 1) (Meyer et al. 2020b)<br>29.4 % (Forbrig et al. 2019)<br>15 % (Pérez-García et al. 2020)<br>24.6 % (Stracke et al. 2020a)<br>20 % (Diana et al. 2021a)<br>100 % (Diana et al. 2021b)<br>58 % (at discharge) and 53 % after 30 days ASSISTENT<br>47.1 % ACUTE |

| | | |
|---|---|---|
| NIHSS | Decrease in NIHSS of 4.5 points from admission to discharge (Meyer et al. 2020a) | Improved non-significantly from 12 to 8 (median) (Stracke et al. 2020b)<br>Improved substantially in 47 % (Forbrig et al. 2019)<br>Improvement from 18 ± 10 to 9 ± 14 (Pérez-García et al. 2020)<br>NIHSS improved from 13 to 6 (median) (Stracke et al. 2020a) |
| Stroke | 5 – 38.2 % (van den Wijngaard et al. 2016; Feng et al. 2017; Gruber et al. 2021) | 6.5 % (peri-procedural), 1.7 % (recurrent) (Meyer et al. 2020b)<br>3.9 % (non-disabling in the region of the target vessel),<br>7.7 % (disabling in the region of the target vessel),<br>3.9 % (disabling outside the region of the target vessel)<br>ASSISTENT |
| Mortality | 3 – 40 % (Feng et al. 2017; Gruber et al. 2021) | 5.2 % (Meyer et al. 2020b)<br>21 % (Forbrig et al. 2019)<br>15 % (Pérez-García et al. 2020)<br>18.5 % (Stracke et al. 2020a)<br>17.1 % (Stracke et al. 2020b)<br>25 % (Diana et al. 2021a)<br>7.7 % ASSISTENT<br>33 % ACUTE |

From the evaluation of the clinical literature, the ACUTE trial and the PMCF study, we can conclude that the technical and clinical success of such medical devices is qualitatively and quantitatively characterized. The performance outcomes of the CREDO Stent are comparable to literature data and therefore non-inferior to the state-of-the-art.

Within the evaluated body of literature stating the use of the CREDO Stent and ACCLINO (flex) Stent in a total of 216 patients respectively, the technical success ranged between 75 % and 100 %. The clinical success described as mTICI ≥ 2b, mRS ≤ 2, NIHSS, stroke and mortality ranged from 29.6 % – 94.5 %, 15 % – 100 %, 4 – 9 points improvement, 3.9 – 7.7 % and 5.2 % – 33 % respectively.

However, for the mTICI score, no range is given from the state-of-the-art. Hence, the values obtained from clinical data can deviate from this single score. Additionally, many of the cited publications describe bail-out stenting in patients with a bad prognosis, hence, single parameters such as the mRS score lie below the value or range given from the state-of-the-art (Forbrig et al. 2019; Pérez-García et al. 2020; Stracke et al. 2020a; Stracke et al. 2020b; Diana et al. 2021a).

**Summary and conclusion:** Regarding the clinical outcome parameters for performance of the CREDO® Stent / ACCLINO® (flex) Stent, it is non-inferior to the state-of-the-art and can thus be considered a state-of-the-art device in its intended purpose.

In conclusion, the CREDO® Stent 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. Recruitment is ongoing until March 2025. An interim PMCF study report after enrollment of 26 patients (in the second study phase) 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.

## 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 harmonized standards and common specifications applied

| Standard | Title | Revision |
|---|---|---|
| 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 10993-11 | Biological evaluation of medical devices - Part 11: Tests for systemic toxicity (ISO 10993-11:2017) | 2018 |
| EN ISO 10993-12 | Biological evaluation of medical devices - Part 12: Sample preparation and reference materials (ISO 10993-12:2021) | 2021 |
| EN ISO 10993-15 | Biological evaluation of medical devices - Part 15: Identification and quantification of degradation products from metals and alloys (ISO 10993-15:2000) | 2009 |
| EN ISO 10993-17 | Biological evaluation of medical devices - Part 17: Establishment of allowable limits for leachable substances (ISO 10993-17:2002) | 2009 |

| Standard | Title | Revision |
|---|---|---|
| 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 10993-2 | Biological evaluation of medical devices - Part 2: Animal welfare requirements (ISO 10993-2:2022) | 2022 |
| EN ISO 10993-23 | Biological evaluation of medical devices - Part 23: Tests for irritation (ISO 10993-23:2021) | 2021 |
| 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 10993-4 | Biological evaluation of medical devices - Part 4: Selection of tests for interactions with blood (ISO 10993-4:2017) | 2017 |
| EN ISO 10993-5 | Biological evaluation of medical devices- Part 5: Tests for in vitro cytotoxicity (ISO 10993-5:2009) | 2009 |
| EN ISO 10993-6 | Biological evaluation of medical devices- Part 6: Tests for local effects after implantation (ISO 10993-6:2016) | 2016 |
| EN ISO 10993-7 | Biological evaluation of medical devices - Part 7: Ethylene oxide sterilization residuals (ISO 10993-7:2008) | 2008 + AC:2009 + A1:2022 |
| 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 11138-1 | Sterilization of health care products - Biological indicators - Part 1: General requirements (ISO 11138-1:2017) | 2017 |
| 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 11139 | Sterilization of health care products – Vocabulary of terms used in sterilization and related equipment and process standards (ISO 11139:2018) | 2018 |
| 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 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 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 14630 | Non-active surgical implants - General requirements (ISO 14630:2012) | 2012 |
| 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 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 14644-3 | Cleanrooms and associated controlled environments - Part 3: Test methods (ISO 14644-3:2019) | 2019 |
| EN ISO 14644-4 | Cleanroom and associated controlled environments - Part 4: Design, construction and start-up (ISO 14644-4:2001) | 2001 |
| EN ISO 14644-5 | Cleanroom and associated controlled environments - Part 5: Operations (ISO 14644-5:2004) | 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 14698-2 | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data TECHNICAL CORRIGENDUM 1 | 2003/ Cor. 1:2004 |

| Standard | Title | Revision |
|---|---|---|
| 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 ISO 25539-1 | Cardiovascular implants – Endovascular devices – Part 1: Endovascular prostheses (ISO 25539-1:2017) | 2017 |
| EN ISO 25539-2 | Cardiovascular implants - Endovascular devices – Part 2: Vascular stents (ISO 25539-2:2020) | 2020 |
| EN 556-1 | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilised medical devices | 2001 + AC:2006 |
| 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 868-2 | Packaging for terminally sterilised medical devices - Part 2: Sterilization wrap – Requirements and test methods | 2017 |

# 2 Information for the patient

Document revision: 02

Date issued: May 15, 2024

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 device. The information presented below is intended for patients or lay persons. An 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 to provide information on the safe use of the device.

## 2.1 Device identification and general information

| | |
|---|---|
| **Device trade name** | CREDO® Stent |
| **Manufacturer's name and address** | Acandis GmbH,<br>Theodor-Fahrner-Straße 6, 75177 Pforzheim, Germany |
| **Basic UDI-DI** | The Unique Device Identification System is a system for the unambiguous identification of medical devices. The Basic UDI-DI for the CREDO® Stent is 426065033CREDO3K. |
| **Year of first CE certificate** | 2015 |

## 2.2 Intended use of the device

| | |
|---|---|
| **Intended purpose** | The CREDO® Stent (a metal mesh) is used to treat narrowed blood vessels in the brain (intracranial stenosis). It is inserted in the narrowed blood vessel and keeps it open after necessary pretreatment. |
| **Indication(s)** | The CREDO® Stent, together with the NeuroSpeed® PTA* Balloon Catheter, is used for expanding (dilatation) the diameter of arteries in the brain (intracranial arteries). This is only possible in arteries that can be reached with the system (stent with PTA balloon catheter). |
| | The device can be used if you<br>- have a narrowing of an artery of over 70 % (high-grade intra-cranial stenoses > 70 %). This may result from a vascular disease (arteriosclerosis) despite intensive drug therapy. You must have signs of limited blood flow to the brain. This is determined by your medical history or laboratory tests and may be seen as a particular pattern of tissue damage caused by poor blood flow and insufficient side vessels (as established clinically, from case history or from laboratory tests), where there is disturbance (hemodynamic infarction pattern and evidence of limited collateral vessels), |

| | |
|---|---|
| | - got symptoms of another stroke despite anti-blood clotting medication (anti-platelet therapy following at least two strokes and not responding to the usual therapy (treatment-refractory),<br>- are over 18 years of age,<br>- had a stroke at least 7 days ago and have a diagnosed impairment after the stroke measured with a specific score ≤ 3 at the time of treatment (3 or less on the modified Rankin scale (mRS)) at the time of treatment.)<br>- have a detected large vessel closure in the brain (intracranial large vessel occlusion (LVO))<br>- have an acute persistent vessel closure (occlusion) resulting from a high-grade narrowing in the brain (intracranial stenosis) for which alternative treatment options are not possible or have failed,<br>- have a suspected underlying stenosis of the closed down artery, that can be treated with a balloon (PTA*) and a stent according to your treating physician (suspected underlying stenosis of the occluded artery, which is suitable (amenable) for expanding with a balloon (PTA) and implanting of a stent (stenting) in the opinion of the treating physician)<br>- have a small to medium infarct core before starting the mechanical surgical removal of the blood clot (with a small to medium infarct core prior to commencement of thrombectomy |
| **Intended patient group** | There is no specific patient group. Your physician decides if the product can be used for your clinical picture or not, considering indications and contraindications |
| **Contra-indications** | The device shall not be used if<br>- the diameter of the healthy vessel before and behind (proximally and distally to) the stenosis does not allow safe treatment with the NeuroSpeed® PTA Balloon Catheter.<br>- the diameter of the healthy vessel before and behind the stenosis does not match the size of the CREDO® Stent.<br>- the diameter of the vessel with the narrowed area after widening (dilatation) does not match the size of the CREDO® Stent.<br>- you cannot be treated with anti-blood clotting medication before the procedure.<br>- you have highly calcified lesions which could prevent access or safe introduction of the stent.<br>- your brain anatomy is unsuitable for treatments inside the vessel as seen in X-rays (Patients who present in the angiography with anatomical conditions unsuitable for endovascular treatment).<br>- you are allergic to nickel-titanium (hypersensitivity). |

* PTA: Percutaneous transluminal angioplasty is a medical procedure to widen narrowed or blocked vessels: The catheter with the small, folded balloon is advanced up to the area of the narrowed blood vessel in the brain. X-rays and contrast agents are used. When correctly placed, the folded balloon is inflated to the desired size. Blockages are pushed aside. When the stenosis is opened, an appropriate stent is implanted in most cases to keep the vessel open. The balloon is retracted.

## 2.3 Device description

### 2.3.1 Description of the CREDO® Stent

The CREDO® Stent is a self-expanding device for the treatment of narrowed blood vessels in the brain (intracranial stenosis). It is available in different sizes. The CREDO® Stent is inserted through a small, flexible hollow tube (NeuroSpeed® PTA Balloon Catheter) that enters the body mostly through a large blood vessel in the groin. From there, the small tube is advanced forward until it reaches the stenosis. The folded stent is advanced through the NeuroSpeed® PTA Balloon Catheter with a transport wire up to the narrowed area in the vessel. For tracing of the device, the device has three markers on both ends which are visible through X-Ray. When correctly placed, the folded device expands itself when it is pushed out of the catheter and the stent attaches to the vessel wall. The transport wire and the catheter are removed.
The CREDO® Stent remains in your body, where it integrates into the vessel wall. After that, the body no longer recognizes the device as a foreign body. You can safely be examined in the MRI. Still, you should inform any physician about the implant.

### 2.3.2 Mode of action

The CREDO® Stent is inserted through a small, flexible hollow tube (NeuroSpeed® PTA Balloon Catheter) that enters the body mostly through a large blood vessel in the groin. From there, the small tube is advanced forward until it reaches the stenosis. The folded stent is advanced through the NeuroSpeed® PTA Balloon Catheter with a transport wire up to the narrowed area in the vessel. For tracing of the device, the device has three markers on both ends which are visible through X-ray. When correctly placed, the folded device expands itself when it is pushed out of the catheter and the stent attaches to the vessel wall. The transport wire and the catheter are removed.

### 2.3.3 Accessories

There are no accessories for the device other than standard operation tools. The device is implanted using the NeuroSpeed® PTA Balloon Catheter.

## 2.4 Risks and warnings

Contact your healthcare professional, if you believe that you are experiencing side effects related to the device, its use or if you are concerned about risks. This document is not intended to replace a consultation with your healthcare professional, if needed. Please take your medicine prescribed by your physician as scheduled, otherwise this can affect the success of the surgery.

### 2.4.1 Residual risks and undesirable effects

Acandis employed a risk management system according to a common industry standard, the ISO (International Organization for Standardization): EN ISO 14971:2019. It is written in the risk management report that the CREDO® Stent is safe for treatment. The medical benefits outweigh the residual risks.

Possible complications are known even when the CREDO® Stent is used according to common knowledge. The physicians are aware of these unwanted effects and can manage them. The most commonly reported complications with 12 patients treated with the CREDO® Stent and 203 with the identical ACCLINO® (flex) Stent were:

- Bleeding within the brain
- Stroke during the procedure or stroke coming back
- Closure of the stent
- Dependency
- Death that could be related to the procedure

In the following, the complete list of possible complications is described:

- General complications in connection with treatments inside the vessel wall (endovascular treatment) and/or treatments with X-rays and contrast agent (angiographic treatments: (e.g. small tears within inner vessel walls with high risk of rupture (pseudoaneurysm), bleeding, bleeding in the brain (intracerebral haemorrhage), blood clotting (embolism), fever, tears or holes in the wall of a blood vessel (vessel dissection, vessel perforation), vessel rupture, narrowing of the vessel (vessel stenosis), vessel injury (vessel trauma), (Abrupt) vessel closure or blood clotting (occlusion or thrombosis, swelling in the brain due to stored fluid (cerebral oedema), sudden increase of arterial pressure (hyperperfusion syndrome), infection, limited blood supply, limited blood supply in the brain ((cerebral) ischemia/infarction), bleeding after the intervention (secondary haemorrhage).
- reactions due to radiation exposure, stroke (thromboembolic event/stroke), contraction of the blood vessel (vasospasm), poisoning).

- General complications in connection with anti-blood clotting drugs (antiplatelet agents/anticoagulants), anesthetics and contrast agents (e.g. renal failing (insufficiency)).
- Complications in connection with the insertion point (vessel entry) (e.g. bruise (hematoma), bleeding, pain or infections at the insertion point of the catheter (puncture site).
- Possible problems when introducing/implanting the stent (e.g. stent breakage, stent folding, incorrect stent placement, stent cannot be released, stent cannot be pulled back into catheter, stent bending, stent does not detach from transport wire, stent movement (migration), insufficient opening, delayed treatment, narrowed area in the vessel (target area) inaccessible or cannot be accessed safely, additional stenting required).
- Other complications in connection with the stent (e.g. allergic reactions to the device material, closure or narrowing of the stent (in-stent stenosis, reoperation), blood clotting or repeated narrowing within the blood vessel (thrombosis, (re)stenosis)), closure of a branch of a blood vessel.
- Deficits of the brain (neurological deficits), e.g. speech impediment (dysphasia), speech disorders, impaired vision, weakening of the eye muscles (oculomotor paresis), weakening or paralysis of one side of the body (hemiparesis or hemiplegia).
- Death (The patients are already very sick when they get the stent.).

### 2.4.2 Warnings and precautions

Acandis gives comprehensive information on warnings, cautions and precautions for the user to ensure a safe and successful implantation of the CREDO® Stent.

In the following, only the patient-related warnings and precautions are listed:

- The CREDO® Stent and the NeuroSpeed® PTA Balloon Catheter should be only used by medical doctors who have the required background knowledge and experience in the minimally invasive treatment of the brain using imaging techniques (interventional neuroradiology) and experience in using stent and balloon catheter to expand narrowed arteries in the brain (stent-assisted percutaneous transluminal angioplasty (PTA)).
- Because application of the PTA balloon catheter involves the risk of blood clotting (subacute thrombosis), vascular complications and/or bleeding, it is necessary to select patients with care.
- As the implantation of stents involves the risk of re-narrowing of the vessel (restenosis), repeat expansion (dilatation) of the vessel section containing the stent may become necessary under certain circumstances. There are currently no findings on the risks

and long-term clinical results of repeat dilatation of stents narrowed with new cells of the blood vessel grown into the stent (endothelialised stents).

- Treatment of narrowed areas in arteries with branched vessels (perforating branches) (e.g. basilar artery)) generally has an increased risk of complications.
- The CREDO® Stent is delivered sterile and for single use only.
- The effect of the pretreatment with anti-blood clotting drugs should be checked before the intervention to minimize potential complications.
- Anti-blood clotting drugs (antiplatelet agent and anticoagulant therapy prior to treatment and anticoagulants during the surgery). should be given in accordance with the current guidelines from the medical societies. If unsuitable drugs are given, this can lead to blood clotting.
- Drugs (the medication) are an important part of stent treatment to avoid potential complications. For this reason, patients should carefully take the prescribed medication (The medication is an important part of the treatment. Patients must be advised by their treating physician to take medication regularly and informed of the potential risks of non-compliance).

### 2.4.3 Other relevant aspects of safety

Since market launch, there were no relevant aspects of safety.

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

Physicians reported on 216 patients who were treated and followed-up with either the CREDO® Stent or the ACCLINO® (flex) Stent. The ACCLINO® (flex) Stent is mechanically identical to the CREDO® Stent and sometimes used alternatively in the treatment of stroke. The reports mention that both the CREDO® Stent and the ACCLINO® (flex) Stent are safe and showed good results in elective stenting of narrowed vessels in the brain and in rescue treatment after acute stroke. This can also be concluded from the two clinical studies (called ACUTE and ASSISTENT) by the manufacturer:

The blood flow was successfully restored in 88.9 % (ACUTE trial), 92 % (ASSISTENT study) and 75 – 100 % (literature). Good results after 90 days were seen in 47.1 % (ACUTE trial), 58 % (ASSISTENT study) and 40 % (literature) of patients. The observed complications were the known complications with such stents and the surgical procedure. The overall complication rate was 27.8 % (ACUTE trial) and 26.9 % (ASSISTENT study) of patients. In the literature, these values are not described in such a way that they can be seen 1:1 as in the studies by the manufacturer. Hence, the safety of the CREDO® Stent seems to be similar to such other stents on the market.

In general, all authors evaluated the CREDO® Stent as a safe and efficient self-expandable, intracranial neurovascular stent for the treatment of blood vessel narrowing and stroke.

Acandis has been conducting the ASSISTENT study since July 2016 which will go on until March 2025.

### 2.6 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.
Treatment alternatives to intracranial stenting include medical management, surgery, mechanical retrieval of the clot from the vessel and PTA without stenting. For each patient it should be evaluated individually, which treatment option is the most promising for good results without impairments. Literature describes that surgery is associated with the least favorable results regarding impairments, whereas mechanical retrieval of the clot is a standard treatment of acute stroke caused by large vessel occlusion. PTA is widely applied in this medical field. Using a balloon and/or stenting was for restoring the vessel patency is feasible in acute large vessel occlusions. The results were favorable in vessel imaging and in results. The safety profile was acceptable but varied from 4 – 40 % within 30 days of treatment. However, secondary narrowing of the vessel is also seen in 24 – 50 % of the patients who received this treatment.

### 2.7 Suggested profile and training for users

The CREDO® Stent and the NeuroSpeed® PTA Balloon Catheter should be only used by physicians who have the required background knowledge and experience in the minimally invasive treatment of the brain using imaging techniques (interventional neuroradiology) and experience in using stent and balloon catheter to expand narrowed arteries in the brain (stent-assisted percutaneous transluminal angioplasty (PTA)).

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