NuMED
Summary of Safety and Clinical Performance
SSCP – Stents - CoA

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

The following information is intended for users/healthcare professionals.

1. Device identification and general information	
Device trade name(s)	NuMED CoA Stent Family CP Stent Mounted CP Stent
Model Number	NuMED CoA Stent Family – Model 1600 CP Stent – Model 425 Mounted CP Stent – Model 426
Manufacturer's name and address	NuMED, Inc. 2880 Main Street Hopkinton, NY 12965 USA
Manufacturer's single registration number (SRN)	US-MF-000010948
Basic UDI-DI	08877141600T2
Medical device nomenclature description / text	EMDN – P070402010102 - METALLIC NON-STAINLESS STEEL CORONARY STENTS
Class of device	III
Year when first certificate (CE) was issued	2004
Authorised Representative (AR)	G. van Wageningen B.V. Hallenweg 40, 5683 CT Best, The Netherlands
AR SRN	NL-AR-000010437
Notified Body	SGS Belgium NV
Notified Body ID number	1639

2. Intended use of the device	
Indications for use	Coarctation of the Aorta (CoA) Indicated for implantation in the native and/or recurrent coarctation of the aorta on patients with the following clinical conditions: • Stenosis of the aorta resulting in significant anatomic narrowing as determined by angiography or non-invasive imaging, i.e. echocardiography, magnetic resonance imaging (MRI), CT scan; • Stenosis of the aorta resulting in hemodynamic alterations, resulting in systolic pressure gradient, systemic hypertension or altered left ventricular function;

	• Stenosis of the aorta where balloon angioplasty is ineffective or contraindicated; • Stenosis diameter <20% of adjacent vessel diameter. Stenosis that would present increased risk of vascular damage or disruption; or aneurysm associated with coarctation of the aorta.
Contraindications and/or limitations	Contraindications include: • Patients too small to allow safe delivery of the stent without compromise to the systemic artery used for delivery; • Unfavorable aortic anatomy that does not dilate with high pressure balloon angioplasty; • Occlusion or obstruction of systemic artery precluding delivery of the stent; • Clinical or biological signs of infection; • Active endocarditis; • Known allergy to aspirin, other antiplatelet agents, or heparin; • Pregnancy.

3. Device description	
Description of the device	The Stents are balloon expandable and intended for permanent implant. The Stents are composed of heat treated 90% platinum/10% iridium wire that is arranged in laser welded rows with a "zig" pattern. The number of zigs in a row can be varied and will impact the strength of the stent as well as the eventual expanded diameter and percent stent shortening, while the number of rows will determine the unexpanded length of the stent. The BIB Stent Placement Catheter is triaxial in construction with two lumens being used to inflate the balloon while one lumen is being used for tracking over a guidewire. The inner balloon is ½ of the outer balloon diameter and 1 cm shorter. The purpose of the double balloon catheter is to apply an incremental inflation for the purpose of dilating a stent. The inner balloon provides initial expansion of the stent and also acts as a tool to hold the stent on the catheter prior to the outer balloon being inflated. The outer balloon is then inflated, providing the remainder of the expansion. There are radiopaque platinum marker bands under the balloon shoulders, to aid during placement. The balloons are designed to inflate to the diameter and length listed on the label at a specific pressure. Thus, it is recommended that the device be used in conjunction with a mechanism to monitor pressure, an inflation device with pressure gauge. The devices are supplied sterile, by ethylene oxide gas, and are intended for single use only. The stents are invasive and intended for permanent implant by an adequately trained/experienced healthcare professional.
Reference to previous generation(s) or variants	N/A
Accessories which are intended to be used in combination with the device	All Stents are designed to be used with the hemostasis valve tools that are provided with the stents.
Description of any other devices and products which are intended to be used in combination with the device	All Stents are designed to be used with a balloon catheter, introducer, and guidewire.

4. Risks and Warning	
Residual risks and undesirable effects	The clinical investigations performed on the CP Stent family of devices reported the following side effects: COAST: aortic aneurysm, stent fracture COAST II: iliac artery dissection The literature reported the following side effects: Acute wall rupture / dissection, aortic aneurysm / pseudoaneurysm, balloon rupture, death, stroke, stent embolization, groin hematoma, late lumen loss, left hemothorax, stent displacement, stent fracture, stent malposition, transitory arrhythmia, and cardiogenic / septic shock. Known and foreseeable clinical risks have been considered in accordance with risk management (RM)

	procedure AP-346 and through the RM files and mitigated as far as possible (AFAP). **POTENTIAL COMPLICATIONS/ADVERSE EFFECTS** NOTE: Circumferential tear of the delivery balloon catheter prior to complete expansion of the stent may cause the balloon to become tethered to the stent, requiring surgical removal. In case of rupture of an adequately sized balloon after stent expansion, it can be withdrawn and a new balloon catheter exchanged over a guidewire to complete expansion of the stent. Cardiac catheterization carries certain risks. Potential complications & adverse effects associated with device use and indication include: - Femoral artery injury, thrombosis or pseudoaneurysm - Stent Migration - Aortic Rupture/Tear - Thrombosis/Thromboembolism - Endocarditis - Stent Stenosis - Stent Malposition - AV fistula formation - Bleeding - Stent Fracture - Hematoma - Death - Cell necrosis at the site of implant - Aortic Aneurysm / Pseudoaneurysm - Sepsis/infection - Transitory arrhythmia - Cerebrovascular Incident
Warning and Precautions	The following Warnings and Precautions have been identified and are called out in the Instruction for Use: **STENT WARNINGS** • Radiofrequency heating during MRI scans on overlapped, 10 zig Stents has not been evaluated. • As with any type of implant, infection secondary to contamination of the stent may lead to aortitis, or abscess. The platinum/iridium stent may migrate from the site of implant. Over-stretching of the artery may result in rupture or aneurysm formation. • When the stent is crimped onto a balloon delivery catheter, the maximum balloon inflation pressure must not exceed the recommended inflation pressure specified in the manufacturer's instructions. • The inflated diameter of the stent should at least equal the diameter of the intended implant site. • Excessive force while crimping may weaken welds of the stent. • Crimping the 8 zig stent on a balloon catheter smaller than 12mm, and the 10 zig on a balloon catheter smaller than 26mm, may cause damage to the stent. • This device is intended for single use only. Do not resterilize and/or reuse it, as this can potentially result in compromised device performance and increased risk of cross contamination. **MOUNTED STENT WARNINGS** • Radiofrequency heating during MRI scans on overlapped, 10 zig Stents has not been evaluated. • As with any type of implant, infection secondary to contamination of the stent may lead to aortitis, or abscess. • The platinum/iridium stent may migrate from the site of implant. • Over-stretching of the artery may result in rupture or aneurysm formation. • The inflated diameter of the stent should at least equal the diameter of the intended implant site. • Excessive force while crimping may weaken welds of the stent. • Crimping the 8 zig stent on a balloon catheter smaller than 12mm, and the 10 zig on a balloon catheter smaller than 26mm, may cause damage to the stent. **BIB STENT PLACEMENT WARNINGS** • Do not exceed the RBP. An inflation device with pressure gauge is recommended to monitor pressure. Pressure in excess of the RBP can cause balloon rupture and potential inability to withdraw the catheter through the introducer sheath. • Confirm that the distal end of the introducing sheath is at least 2.5cm back from the most proximal image markers before inflating the outer balloon. Failure to do so may stretch the outer tubing and severely hinder balloon deflation. • Use two appropriate size inflation devices with pressure gauges for inflation. • Do not advance the guidewire, balloon dilatation catheter, or any other component if resistance is met,

	without first determining the cause and taking remedial action. • This catheter is not recommended for pressure measurement or fluid injection. • Do not remove the guidewire from the catheter at any time during the procedure except when the procedure has been completed. • This device is intended for single use only. Do not resterilize and/or reuse it, as this can potentially result in compromised device performance and increased risk of cross contamination. **STENT PRECAUTIONS** • Use of an inflation device with pressure gauge is highly recommended during this procedure. • The stent is rigid and may make negotiation through vessels difficult. • Dilatation procedures should be conducted under fluoroscopic guidance with appropriate x-ray equipment. • Guidewires are delicate instruments. Care should be exercised while handling to help prevent the possibility of breakage. • Careful attention must be paid to the maintenance of tight catheter connections and by aspiration before proceeding to avoid air introduction into the system. • Under no circumstances should any portion of the catheter system be advanced against resistance. The cause of the resistance should be identified with fluoroscopy and action taken to remedy the problem. **MOUNTED STENT PRECAUTIONS** • Use of an inflation device with pressure gauge is highly recommended during this procedure. • Stents are delicate devices. Care should be exercised while handling to help prevent the possibility of breakage. • The stent is rigid and may make negotiation through vessels difficult. • Dilatation procedures should be conducted under fluoroscopic guidance with appropriate x-ray equipment. • Guidewires are delicate instruments. Care should be exercised while handling to help prevent the possibility of breakage. • Careful attention must be paid to the maintenance of tight catheter connections and by aspiration before proceeding to avoid air introduction into the system. • The inflation diameter of the balloon used during stent delivery should approximate the diameter of the obstructive vessel and the intended implant site. • Under no circumstances should any portion of the catheter system be advanced against resistance. The cause of the resistance should be identified with fluoroscopy and action taken to remedy the problem. • If resistance is felt upon removal, then the balloon, guidewire and the sheath should be removed together as a unit, particularly if balloon rupture or leakage is known or suspected. This may be accomplished by firmly grasping the balloon catheter and sheath as a unit and withdrawing both together, using a gentle twisting motion combined with traction. • The balloons must be completely deflated before retracting into the sheath. • Proper functioning of the catheter depends on its integrity. Care should be used when handling the catheter. Damage may result from kinking, stretching, or forceful wiping of the catheter.
Other relevant aspects of safety, including a summary of any field safety corrective actions (FSCA including FSN) if applicable	Since commercialization, there has been one recall on the Bare CP Stent in 2003 (#Z-0983-03, completed in 2004) concerning the lack of PMA or 510(k) for the Bare CP Stent. The recall was conducted in the U.S. only. There have not been any Field Safety Corrective Actions or Field Safety Notices on any other version of the Stents.

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

Summary of clinical data related to equivalent device:

An equivalent device was not used for the clinical evaluation.

Summary of clinical data from conducted investigations of the device:

1. Study name: COAST

Purpose: to provide information that will support labeling of both the CP bare metal and covered stents to treat native and recurrent CoA in selected children, adolescents and adult.

Clinical Study Methodology: Single arm interventional study (open label). The COAST is a prospective, multicenter, single-arm clinical study involving 19 pediatric cardiology centers in the United States. The study includes patients with native or recurrent CoA treated by physicians at the participating institutions. A total of 105 patients underwent attempted implantation, with 104 successes.

Reference to the clinical study plan (and amendment) n°: NCT00552812

Investigation site: 19 pediatric cardiology centers in United States

Ethics Committee Approval: Institutional Review Board approvals from all participating institutions

Regulatory Authority Approvals: Investigational Device Exemption from US FDA (August 3, 2007)

Patient Population: Patients with native or recurrent CoA. A total of 105 patients underwent attempted implantation, median age 16 years (range from 8 to 52 years) and with 69.5% male.

Clinical Study Results: Results held on file by Sponsor

Purpose	Criteria	Results
Performance	Blood pressure gradient and coarctation minimum diameter: cardiac catheterization before and after CP Stent placement	Average systolic blood pressure difference (mmHg) changed from 29±14 mmHg at baseline to -3±15 mmHg at 24 months follow-up. The Coarctation minimum diameter reported at 7.9 ± 2.7mm at baseline to 14±3 mm after implantation.
Safety	Adverse events	No serious adverse events reported, 7% of the patients experienced somewhat serious events. Aortic aneurysms (n=6): 5 were successfully treated with covered stent placement, and 1 resolved without intervention. Stent fractures were seen in 2 patients after one year, 11 patients at two years and 12 additional fractures above 2 years.

Reference to the Clinical Study Report n°: NCT00552812

Device Used: Bare CP Stent and BIB catheter; covered stents were available in case of aortic wall injury.

Conclusion: The CP stent is safe and associated with persistent relief of aortic obstruction. Stent fracture and progression of fracture occur but have not resulted in clinically important sequelae. Reintervention is common and related to early and late aortic wall injury and need for re-expansion of small-diameter stents.

Summary of clinical data from other sources:

First Author (Year)	Appraisal/Results
1. Baykan et al. (2018)	**Safety & Performance (safety only)**

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Control study. Study group was composed of 20 CoA patients who were treated with CP Stent between the dates October 2008 and February 2015, and control group was composed of 20 healthy children with age and sex matched.	To address the presence of hypertension and risk for cardiovascular diseases in patients with CoA who were treated with endovascular stent placement.	1	2	**3**	4	5

Suitability	Relevant Data	Grading		
Device	- CP Stents (Bare and Covered)	**D1**	D2	D3
Application	- CoA	**A1**	A2	A3

Patient	- Patients who had undergone stent placement for CoA compared with control group (healthy children with age and sex matched).
	- Sampling: n=20 CoA and n=20 healthy children
	- Mean age:
	  - CoA group: 14.2 (SD: 3.9) years
	  - Control group: 13.7 (SD: 2.7) years
	- Sex:
	  - CoA group: 16M; 4F
	  - Control group: 15M; 5F
		P1	P2	P3

Report	- High quality	**R1**	R2	R3
	Suitability Grade (Range 4-12)	4		

Contribution	
S&P	X (safety only)
SOA	

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Ambulatory blood pressure	**Yes 1**	No 2
Follow-up	- 6 months and 6 years	**Yes 1**	No 2
Statistical analysis	- Student t-test was used if the two independent group comparisons were normal and the Mann-Whitney U test was used if the normal distribution was not present. Pearson chi-square analysis was performed to determine whether there was a difference in categorical variables between the case and control groups.	**Yes 1**	No 2
Clinical significance	- It was shown that hypertension incidence as demonstrated by ambulatory blood pressure monitorization and risk for cardiovascular diseases as indicated by carotid intima media thickness and pulse wave velocity were higher than those in healthy population even after CoA is corrected. - CoA should be carefully monitored for hypertension, even if it has been completely corrected	**Yes 1**	No 2

	by any method. This study suggests that CoA is a part of generalized vasculopathy rather than being a localized narrowing.		
		Data Contribution Grade (Range 4-8)	4

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (3) + Suitability (4) + Data Contribution (4) = 11	Disposition and Weighting (select)	**Accepted and Pivotal 9-12** Accepted but not Pivotal, 13-21 Excluded, 22-25

Relevant S&P Results

Safety data	- Hypertensive:
	  - Daytime: 5% were hypertensive and 20% were pre-hypertensive in the study group compared to 0% in the control group.
	  - Night: 15% were hypertensive and 15% were pre-hypertensive in the study group compared to 0% in the control group.

Performance data	- Mean arterial pressure:
	  - At 24 hours: 88.5 (81-96) mmHg in study group and 83 (80-86) mm Hg in control group
	  - Daytime: 91 (84-99) mmHg in study group and 84 (81-88) mmHg in control group
	  - Night: 78 (76-87) mmHg in study group and 78 (75-81)mmHg in control group

Benefits/claims data	- N/A
Strengths	- N/A
Weaknesses/ Potential bias	- Patients were treated only with "NuMED brand Bare and Covered Stent" types. In the future the authors can do more extensive studies with more cases and different types of stents. - Same methodology (blood pressure monitoring with Holter device) in pre-operative period could not be used because at that time they did not have a blood pressure Holter device.

2. Sohrabi et al. (2014)

Contribution	
S&P	X (safety only)
SOA	

Safety & Performance (safety only)

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Prospective randomized controlled trial.	To evaluate outcomes of treatment with Covered versus Bare NuMED CP Stents.	1	**2**	3	4	5

Suitability	Relevant Data	Grading		
Device	- NuMED CP Stent (Bare and Covered) - BIB	**D1**	D2	D3
Application	- Severe native CoA	**A1**	A2	A3
Patient	- Patients with severe native CoA - Sampling: n=120 (60 CP Stents versus 60 CP Stents, Covered) - Mean age: 23.6±10.99 (range 12 to 58) years - Sex: 79 M; 41 F	**P1**	P2	P3
Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	4		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Procedural success - Reduction in systolic blood pressure gradient - Reduction in mean diameter of coarctation segment - Adverse effects	**Yes 1**	No 2
Follow-up	- 31.1 ± 19.2 months	**Yes 1**	No 2
Statistical analysis	- A p-value <0.05 was considered significant.	**Yes 1**	No 2
Clinical significance	- Implanting CP Stent (Bare) and CP Stent (Covered) have very high success rates with remarkable hemodynamic effects in severe native CoA patients, with no significant complication during the procedure and hospitalization. - Patients undergoing CP Stent (Covered) implantation experienced a non-significantly lower re-coarctation rate and a higher occurrence of pseudoaneurysm formation with respect to CP Stent (Bare) stenting during follow-up. - In both groups, blood pressure was significantly reduced after intervention. - These findings indicate that CoA stenting is a safe procedure.	**Yes 1**	No 2
	Data Contribution Grade (Range 4-8)	4	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (2) + Suitability (4) + Data Contribution (4) = 10	Disposition and Weighting (select)	**Accepted and Pivotal 9-12** Accepted but not Pivotal, 13-21 Excluded, 22-25

Relevant S&P Results

Safety data	- Pseudoaneurysms: 0 (CP Stent, Bare) versus 2 (CP Stent, Covered) - Mortality: 1 (CP Stent, Bare) versus 0 (CP Stent, Covered)
Performance data	- Successful placement: successful in all patients - Mean systolic blood pressure gradient reduction: from 54.61 (CP Stent, Bare) and 54.42 (CP Stent, Covered) to 3.47 and 3.36 mmHg respectively; no significant difference between the two types of stent, P<0.001 - Mean diameter of coarctation segment reduction: From 3.34 (CP Stent, Bare) and 3.30 (CP Stent, Covered) to 16.07 and 15.82 mm respectively; no significant difference between the two types of stent, P<0.001 - Recurring coarctation: 4 (CP Stent, Bare) versus 0 (CP Stent, Covered), non-significant
Benefits/claims data	- Reduction in mean systolic blood pressure gradient - Reduction in diameter of coarctation segment
Strengths	- The CP Stent was hand-crimped down onto a balloon-in-balloon catheter (NuMED), which allows a precise and safe stent delivery
Weaknesses/ Potential bias	- Although the first randomized clinical trial in this respect, study was limited in some aspects. First, during follow-up, patients did not undergo 24-hour ambulatory blood pressure monitoring, which could have diagnosed the normotensive state more accurately. Second, evaluation of the blood pressure response during exercise testing could have been more valuable in defining the procedure outcome. -

3. Erdem et al. (2011)

Contribution	
S&P	X (safety only)
SOA	

Safety & Performance (safety only)

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Single arm interventional study.	To present author's institutional experience of endovascular CP Stent implantation in children and adults with native and recurrent CoA.	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	- CP Stent (16 Covered or 31 Bare) – n=47 - BIB (n=29) or single balloon catheter (n=18), Z-med (not subject device)	D1	**D2**	D3
Application	- Patients with native or recurrent CoA	**A1**	A2	A3
Patient	- Patients with native CoA (Group 1); recurrent CoA and/or aneurysm developed after either surgery or balloon angioplasty (Group 2) - Sampling: n=45 (47 CP Stents, Covered or Bare) - Median age: 11 (range: 5-33) years - Sex: 34M; 11F	**P1**	P2	P3
Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	5		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Decrease in invasive and echocardiographic gradients - Increase in lesion diameter - Adverse effects	**Yes 1**	No 2
Follow-up	- 12.1±7.1 months; median 11 month (range 2-29)	**Yes 1**	No 2
Statistical analysis	- A p value <0.05 was considered statistically significant.	**Yes 1**	No 2
Clinical significance	- Early and short- term follow-up results indicate that stent implantation is safe and very effective in reducing coarctation gradient and increasing lesion diameter both in native and recurrent CoA. - Some serious complications do occur and hypertension remains in some patients. - Aortic disruption and stent displacement are potentially catastrophic complications of stenting but implanting a second covered stent can seal the ruptured wall and parking in a safe area or replacement of displaced stent carried by half-inflated balloon could solve the problem.	**Yes 1**	No 2
	Data Contribution Grade (Range 4-8)	4	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (4) + Suitability (5) + Data Contribution (4) = 13	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant S&P Results

Safety data	- No procedure related death.
	- Two immediate complications relating to stenting:
	  - One an acute wall rupture, successfully managed immediately in the same session with implantation of a second covered stent
	  - One stent was displaced before it was completely opened. It was carried with support of partially inflated balloon and long sheath, and repositioned into the correct place.
	- No femoral arterial complications
	- No difficulty in catheter manipulation.
	- None of the patients required intensive care following the procedure, and all were discharged home the following day except the patient with aortic rupture and after stenting with covered stent this patient was followed two days in intensive care unit.

Performance data	- Considering all cases, a statistically significant decrease in both the invasive and echocardiographic gradients ($p<0.001$ for both) - Statistically significant increase in lesion diameter ($p<0.001$) were detected. - Before the procedure, the invasive gradient was significantly higher and the lesion diameter was significantly lower in Group I than in Group II ($p=0.002$ and $p=0.005$, respectively). - Percentage of decrease in gradient and increase in diameter was statistically higher in group 1 than in group 2 ($p=0.04$ and $p=0.04$). - When the stent was in good position, the balloon was inflated to fix the stent in the coarctation site.
Benefits/claims data	- Increase in luminal/lesion diameter.
Strengths	- CP stent is the one of the most commonly used stent in pediatric cardiology - This stent has excellent radial strength even at larger diameters and also has brilliant visibility on fluoroscopy.

Weaknesses/ Potential bias	- Some limitations have to be noted about this study:
	  - Firstly, there is a need a greater number of patients have undergone stent implantation and their long-term results.
	  - Secondly, population included both children and adult.
	  - Thirdly, this was a single-center report and patients were not compared with surgery or balloon angioplasty alone.
	  - Fourthly, 24-hour ambulatory blood pressure monitoring before stenting was not performed in any patients.
	  - Finally, radiologic imaging for aneurysm was done in limited number of patients after procedure.
	- Conflict of interest: None declared.

4. Moltzer et al. (2010)

Contribution	
S&P	X (safety only)
SOA	

Safety & Performance (safety only)

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Prospective observational study.	To evaluate the intermediate-term outcome of stent implantation for CoA in adults.	1	2	**3**	4	5

Suitability	Relevant Data	Grading		
Device	- CP Stent (Bare and Covered) - BIB	**D1**	D2	D3

Application	- Native CoA and re-coarctation	**A1**	A2	A3
Patient	- Patients with native CoA and re-coarctation - Sampling: n=24 - Mean age: 36 (18-60) years - Sex: 12 M; 12 F	**P1**	P2	P3
Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	4		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Decrease in systolic gradient - Increase in minimum aortic diameter - Adverse effects	**Yes 1**	No 2
Follow-up	- 24 hours post intervention and 33 (8-77) months	**Yes 1**	No 2
Statistical analysis	- All statistical tests were two-sided and a p-value <0.05 was considered statistically significant	**Yes 1**	No 2
Clinical significance	- Stenting in adults results in significant blood pressure gradient decrease and increase in vessel diameter. However, serious complications do occur and hypertension remains in the majority of patients.	**Yes 1**	No 2
	Data Contribution Grade (Range 4-8)	4	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (3) + Suitability (4) + Data Contribution (4) = 11	Disposition and Weighting (select)	**Accepted and Pivotal 9-12** Accepted but not Pivotal, 13-21 Excluded, 22-25

Relevant S&P Results

Safety data	- One death due to aorta ruptured. - Two groin hematoma post-op.
Performance data	- Systolic gradient: Decreased to < 10 mmHg in 21 patients, P<0.001 - Minimum aortic diameter: Increased from median 10 (2-17) to 16 (10-28) mm, P<0.001
Benefits/claims data	- Reduced in systolic gradient - Increased in minimum aortic diameter
Strengths	- N/A
Weaknesses/ Potential bias	- Only a small number of patients have undergone stent implantation since the authors started this procedure in 2003. This was a single-center report and patients were not compared with surgery or balloon angioplasty alone. Finally, 24-hour blood pressure monitoring before stenting was not performed in the majority of the patients. Post-stent 24-hour ambulatory blood pressure monitoring is therefore difficult to translate in terms of blood pressure reduction.

5. Agnoletti et al. (2009)

Contribution	
S&P	X (safety only)
SOA	

Safety & Performance (safety only)

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Two arms comparative interventional study.	To compare the CP Stent and the Palmaz stent for treatment of native and postoperative lesions of CHD patients.	1	2	**3**	4	5

Suitability	Relevant Data	Grading		
Device	- CP Stent (Bare & Covered), crimped on BIB - Palmaz stent, crimped on BIB and simple balloons	**D1**	D2	D3
Application	- Patients with CHD (including CoA/re-coarctation, RVOT)	A1	**A2**	A3

Patient	- Patients with CHD (including CoA/re-coarctation, RVOT and other CHD conditions, such as transposition of the great arteries, ventricular septal defect, single ventricle, etc.)
	- Sampling: n= 153
	  - 89 CP Stents (crimped on 77 BIB & 12 other balloons)
	  - 64 Palmaz Stents (crimped on 23 BIB and 41 simple balloons)
	- Mean age:
	  - CP Stents: 15.4 (SD: 9.2) years
	  - Palmaz Stents: 11.6 (SD: 8.1) years
	- Sex: Not reported
		P1	**P2**	P3

Report	- High quality.	**R1**	R2	R3
	Suitability Grade (Range 4-12)	6		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Blood pressure gradient reduction - Vessel diameter reduction - Adverse effects	**Yes 1**	No 2
Follow-up	- Not reported.	Yes 1	**No 2**
Statistical analysis	- A P-value less than 0.05 was considered statistically significant for stent group comparison.	**Yes 1**	No 2
Clinical significance	- The use of the CP Stents to treat stenotic lesions of CHD is effective and relatively safe. The overall efficacy of CP Stents for the treatment of stenotic lesions is superior to that of the Palmaz stent. - CP Stents' overall safety is higher than that of the Palmaz stent; but Palmaz stents have a lower profile when inserted.	**Yes 1**	No 2
	Data Contribution Grade (Range 4-8)	5	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (3) + Suitability (6) + Data Contribution (5) = 14	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant S&P Results

Safety data	- Stent-related complications:
	  - CP Stents (n=89 patients): 4 mild, 1 moderate, 1 severe.
	  - Palmaz (n=64 patients): 10 mild, 2 moderate, 2 severe.
	- Stent migration:
	  - CP Stents: 7.
	  - Palmaz: 4.
	- Non stent related complications:
	  - CP Stents: 1 mild, 2 moderate.
	  - Palmaz: 1 mild, 2 moderate, 5 severe.
	- Urgent surgery:
	  - CP Stents: 2 due to homograft rupture and stent migration.
	  - Palmaz: 1 for aortic dissection.
	- Balloon related complications: Balloon burst
	  - CP Stents: 0.
	  - Palmaz: 7 (3 in BIB, 3 with simple balloons, and 1 on pre-mounted stent).

Performance data	- Blood pressure gradient reduction (P<0.004)
	  - CP: from 45.4 ± 25.7 to 8.7 ± 15.7 mmHg.
	  - Palmaz: from 37.7 ± 28.3 to 12.3 ± 15.1 mmHg.
	- Vessel diameter (P<0.002)
	  - CP: from 7.4 ± 2.6 to 13.3 ± 3.4 mm.
	  - Palmaz: from 5.8 ± 2.7 to 13.3 + 4.5 mm.

Benefits/claims data	- Decreased in blood pressure gradient. - Increased in vessel diameter.
Strengths	- Efficacy of CP Stents was similar to that of Palmaz stent for stenting of the right ventricular outflow, and higher than that of Palmaz for the stenting of aorta, but the difference was not statistically.
Weaknesses/ Potential bias	- Study presented retrospective results obtained in 153 consecutive patients. - CP stents were used for patients weighing more than 15 kg; and thus two populations were different concerning age, weight, indication for stenting; however, none of these differences were related to occurrence of complications. - Subgroup analyses were not performed.

6. Meadows et al. (2015)

Contribution	
S&P	x
SOA	

Safety & Performance

This publication presents the results from the COAST trial for CP Stent (Bare and Covered) to treat native and recurrent CoA in selected children, adolescents and adult (NCT00552812). Please refer information presented in **Table G-1** for safety and performance of the subject devices, Study no. 1.

7. Sasikumar et al. (2020)

Contribution	
S&P	X (safety only)
SOA	x

Safety & Performance (safety only)

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Retrospective study.	To study the early and late outcomes after stenting of native and recurrent CoA with uncovered and covered stents.	1	2	**3**	4	5

Suitability	Relevant Data	Grading		
Device	- CP Stent (Bare and Covered) – "D1" for subject devices - Other devices, including Advanta V12 stent (covered), Andra XL and XXL stents, Palmaz XL	**D1**	D2	D3
Application	- CoA (native and recurrent)	**A1**	A2	A3

Patient	- Patients with CoA (native and recurrent)
	- Sampling: n=45 (20 covered stents, 25 non-covered stents)
	  - Covered stents used were covered 7 CP Stent; 13 Advanta V12 Stent
	  - Non-covered stents used were 17 CP Stent, 6 Andra XL and XXL stents, and 2 Palmaz XL.
	- Mean age: 28±17.5 (range 8 to 65) years. Age per device group was not reported.
	- Sex: 32 M, 13 F. Sex per device group was not reported.
		P1	**P2**	P3

Report	- High quality with deficiencies	R1	**R2**	R3
	Suitability Grade (Range 4-12)	6		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Safety	**Yes 1**	No 2
Follow-up	- Covered stent group: 57 months - Non-covered stent group: 35 months	**Yes 1**	No 2
Statistical analysis	- Statistical analysis was done by the Statistical Package for Social Sciences (version 21.0). Quantitative data were presented as mean ± SD or as median and range and qualitative data were presented as frequency (percentages). The categorical parameters were compared by chi-square test, and the continuous variables were compared by Student t test for independent continuous data and Manne Whitney U test for nonparametric data.	**Yes 1**	No 2
Clinical significance	- Not reported specifically for subject devices.	Yes 1	**No 2**
	Data Contribution Grade (Range 4-8)	5	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (3) + Suitability (6) + Data Contribution (5) = 14	Disposition and Weighting (select)	Accepted and Pivotal 9-12 **Accepted but not Pivotal, 13-21** Excluded, 22-25

Relevant S&P Results

Safety data	**Outcomes**	**Covered (n=18)**	**Uncovered (bare metal) (n=8)**

	Late lumen loss (no or mild)	2 (Advanta 1, CP 1)	4 (CP 3, Palmaz 1)
	Late lumen loss (moderate)	12 (Advanta 7, CP 4, Andra 1)	4 (CP3, Palmaz 1)
	Late lumen loss (severe)	4 (Advanta 3, CP 1)	0
	Fracture	1 Advanta	0

Performance data	- Not reported specially for subject devices.
Benefits/claims data	- Not reported
Strengths	- Not reported.
Weaknesses/ Potential bias	- Not reported.

State of the Art

Appraisal

Medical condition		Alternatives		Risk/benefit		Side-effects		Equivalence		Surrogate endpoints	
Yes 1	No 2	**Yes 1**	No 2	**Yes 1**	No 2	**Yes 1**	No 2	Yes 1	**No 2**	Yes 1	**No 2**

Overall SOA Appraisal and Disposition

SOA Grade (Range 6-12)	8	Disposition (select)	**Accepted, < 12** Excluded, 12

Relevant SOA Results

SOA data	- Patients in the covered stent group were older and had greater basal pressure gradient. More patients in the covered stent group had residual gradient >10 mm Hg after the procedure. - No mortality or aortic wall injury in either group. - Mean number of anti-hypertensive was 1.38 ± 0.74 in the covered goup and 1+0.7 in the uncovered group - Greater incidence of severe late lumen loss (>30% lumen loss) in the covered stent group on follow-up. According to the authors, this phenomenon was brand specific (Advanta V12 stent). Single strut fracture which was not causing any lumen obstruction was also noted in one Advanta V12 stent. The stents have an open cell stent geometry with consequent less radial strength. - A previous study on Advanta stent implantation in 25 patients did not show any complications related to the stent. However, the median period of follow-up in that study was only 4.9 months and longer follow-up is needed to look for re-coarctation or aneurysm formation. - Another study described 2 patients with Advanta stent implantation who developed in-folding of the proximal edge of the stent on follow-up and both the cases were managed by re-stenting. The authors had a similar proximal stent collapse in a patient who had Advanta stent implantation, which was managed by balloon angioplasty. Though the residual gradient was 5 mm Hg immediately after the balloon angioplasty, the gradient increased to 25mmHg on follow-up and he underwent a repeat balloon angioplasty with good result.

Comments	- Uncovered stents can be safely implanted with minimal risk of aortic wall injury in patients with low risk anatomic features. Covered stent implantation is associated with higher incidence of planned and unplanned re-intervention.

Safety & Performance (safety only)

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Included in this report are the 5-year follow-up data from patients in these 2 trials and those treated through their Continued Access protocols. Data was prospectively collected during the 2 multi-center studies.	To report the late-term follow-up data and to compare this to earlier follow-up data. For the purpose of this study, follow-up was defined as: - Immediate (1 month), - Early (12 months), - Late (48 or 60 months). To identify possible predictors of late-term outcome post-stent implantation.	1	2	**3**	4	5

8. Holzer et al. (2021)

Contribution	
S&P	X (safety only)
SOA	x

Suitability	Relevant Data	Grading		
Device	- CP Stent (Bare and Covered) - 52% received covered stents and 48% received bare stents. - The minimum stent diameter was 14.4mm (interquartile range (IQR), 12.6-16.0mm) with a minimum stent diameter to the aorta at diaphram ratio of 0.87 (IQR, 0.77-1.0).	**D1**	D2	D3
Application	- CoA (native or recurrent) - Native coarctation was present in 49%, postsurgical in 24% and post-catheterization in 27%. - The minimum coarctation diameter was 8.0mm (IQR, 5.4-10.5mm), and median aortic diameter at the diaphragm was 16.0mm (IQR, 14.0-19.0mm).	**A1**	A2	A3
Patient	- All patients enrolled in the COAST or COAST II trials and their Continued Access extensions were included. Patients without late follow-up data were excluded from analysis, except for analyzing the estimated cumulative incidence of stent fractures, aortic wall injury, and reinterventions. - Cohort of 248 patients - COAST: 105 patients enrolled in COAST with 16 Continued Access patients (n=121) - COAST II: 82 participants from COAST II with an additional 45 Continued access patients (n=127). - From the 180 patient cohort, the median age at implant was 17 years (IQR, 13-28 years), the median weight (66.3kg, IQR, 53.8-78.1kg).	**P1**	P2	P3
Report	- High quality report	**R1**	R2	R3
	Suitability Grade (Range 4-12)	4		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	- Parameters used to assess aortic stent outcomes: -Hemodynamic	**Yes 1**	No 2

		-Systemic systolic hypertension -Use of antihypertensive medication -Upper limb to lower limb blood pressure difference of ≥20mm Hg -Reinterventions -Stent fractures -Aortic wall injury - Predictor variables used to assess late-term results: -Demographics -Type of coarctation -Preimplantation clinical data -Baseline characterization data -Type of stent -Poststent catherization data -Postcatheterization data		
	Follow-up	- Follow-up data was collected at 1, 6, 12, 24, 36, 48 and 60 months and included MRI at 12 and 24 months, and fluoroscopy at 12, 24, 48 and 60 months. - 96% of patients returned for 1-month follow-up, 86% for 12-month follow-up, and 63% for 60-month. - A total of 180 patients (73%) had either 48- or 60-month follow-up data. - Out of the 180 patients with late follow-up, 177 (98%) had also immediate and 180 (100%) early follow-up data available for analysis. - Aortic imaging (either MRI, computed tomography, or angiography) was available for 180/180 (100%) at immediate follow-up, 177/180 (98%) at intermediate follow-up, and 41:180 (23%) at late follow-up. Fluoroscopy was available for 180/180 (100%) at immediate follow-up, 178/180 (99%) at intermediate follow-up, and 136/180 (76%) at late follow-up.	**Yes 1**	No 2
	Statistical analysis	- Categorical variables are summarized as frequencies and percentages, and continuous variables as either means and SDs or medians with interquartile range (IQR) as noted. For the entire cohort, the cumulative incidence of stents fractures, aortic wall injury, and reinterventions at immediate, early and late follow-up was estimated using the Kaplan-Meier method. Patients who did not have an outcome event were censored at time. Changes in hemodynamic measures over time were evaluated using tests of trend. For patients with late follow-up, associations between patient and procedure characteristics and 4 binary outcome variables – suboptimal hemodynamic outcome, stent fractur, catheter reintervention, and aortic wall injury – were assessed using Fisher exact test. Characteristics significant at the 0.20 level were considered for inclusion in multivariable logistic regression models. Forward selection was used, and $P < 0.05$ was required for retention in the final model. To assess generalizability, characteristics of patients with and without late follow-up were compared using Fisher exact and Wilcoxon rank sum tests; no significant differences were found. All analytics were performed using SAS software version 9.4.	**Yes 1**	No 2
	Clinical significance	- Coarctation stenting is effective at maintaining obstruction relief up to 60 months postimplant	**Yes 1**	No 2

	with reduction in the number of patients requiring antihypertensive medication. However, an increase in-stent fractures and reinterventions were observed between medium and long-term follow-up. Covered stents appear to confer some protection from the development of stent fractures but do not provide complete protection from late aneurysm formation.		
		Data Contribution Grade (Range 4-8)	4

Overall S&P Appraisal, Disposition and Weighting

S&P Grade (Range 9-25)	LOE (3) + Suitability (4) + Data Contribution (4) = 11	Disposition and Weighting (select)	**Accepted and Pivotal 9-12** Accepted but not Pivotal, 13-21 Excluded, 22-25

Relevant S&P Results

Safety data	Aortic Wall Injury: - 13 patients were identified as having aneurysms or pseudo-aneurysms (COAST: 6/121 [5%], COAST II: 7/127 [5.5%]. - No dissections were found. - The cumulative incidence was 1.2% by early and 6.3% by late follow-up. - In 3 patients, the aneurysm was proximal to the implanted stent, in one patient the location was not specified, and in the reminder, the aneurysm was within the borders of the implanted stent. - In 4 of 13 patients, aneurysms were identified on MRI or computed tomography before reintervention, while in 9 patients the aneurysms were diagnosed by angiography during catheterization performed for other reasons such as elective stent re-expansion. - 17 patients had covered stents implanted to treat the aneurysm; 2 did not. - By univariate analysis, coarctation minimum diameter <6mmm was the only factor significantly associated with aortic wall injury (12% versus 2%, P=0.007). - There was a borderline relationship between minimum stent to aortic diameter at the diaphragm <0.7 and aortic wall injury (19% versus 5%, M=0.059). - Aneurysms did not just occur in patients with bare metal stents, but equally in patients who had covered stents implanted. As such, the notion that covered stent implantation confers long-term protection from the development of aneurysm, may not be the case. Data are in contrast with Butera et al.[1] who did show a significant difference in the incidence of aneurysm formation when comparing patients bare versus covered stents, albeit in a much smaller cohort. Also, the median follow-up in that study was significantly longer for those with bare stents compared with covered stents (85 versus 35 months). This is important as the current study demonstrates that the majority of aneurysms were not identified until late follow-up. - Most aneurysms developed within the borders of the stent, including covered stents. One possible explanation is that pressure within the aorta distributes flow between the stent and the aortic wall, eventually leading to aneurysm formation. Another possibility is that the expanded polytetrafluoroethylene became damaged during initial implantation. - Current study did not investigate the benefit of a covered stent to reduce the risk of acute aortic wall injury during stent implantation because cases have not been randomly assigned and high-risk patients were excluded for bare

[1] Butera G, Manica JL, Marini D, Piazza L, Chessa M, Filho RI, Sarmento Leite RE, Carminati M. From bare to covered: 15-year single center experience and follow-up in trans-catheter stent implantation for aortic coarctation. Catheter Cardiovasc Interv. 2014 May 1;83(6):953-63. doi: 10.1002/ccd.25404. Epub 2014 Feb 4. PMID: 24459104.

	stent implantation and received covered stents. Other Adverse Events: - Over the follow-up period, 2 patients had additional adverse events that were captured in the data set. One patient had a self-resolving neurological adverse event (possible transient ischemic attack) 2 weeks after the procedure without any clear relationship to the procedure itself. Another patient developed cardiogenic/sceptic chock 7 months after the procedure. No other serious adverse events were documented in any patients.
Performance data	Hemodynamic Outcome: - The number of patients with suboptimal hemodynamic outcome was 59% at immediate and early follow-up and decreased to 44% at late follow-up (P=0.001; median age, 21.7 years). - When comparing immediate, to early and late follow-up, there was no significant difference in SBP. Hypertension remained fairly constant at about 20% of patients. - Systolic arm-leg blood pressure gradients did not change significantly between immediate, early and late follow-up (median of -1 to -2mm Hg) with 91% to 95% <20mm Hg, 85% to 89% <15mm Hg, and 77% to 80% <10mm Hg. - There was a significant decrease in use of hypertension medication, from 53% at immediate, to 42% at early, and 29% at late follow-up (P<0.001). - By univariate analysis, none of the predictor variables had a significant association with suboptimal hemodynamic outcome at late follow-up. - No association was found between the ratio of minimum stent diameter to aortic diameter at the diaphragm <0.7, and residual arm-leg SBP gradients >10, 15, or 20mm Hg at late follow-up. Stent Fractures: - There were 50 patients with stent fractures. - The cumulative incidence was 0% by immediate, 2.9% by early, and 24.4% by late follow-up. - There were no stent segment embolization and no complete circumferential or longitudinal stent fractures. - The CP stent fractured in multiple locations leading to loss of stent integrity in only 3 patients. - No patient with stent fracture had a reintervention at immediate or early follow-up, but 12 had reinterventions at late follow-up (estimated incidence 6.0%. - By multivariate analysis, independent predictors of stent fracture by late follow-up were age: < 18 years (odds ratio [OR], 3.33 [95%CI, 1.38-8.03], P=0.008), male sex (OR, 3.11 [95% CI, 1.15-8.47], P=0.026), minimum stent diameter at implantation ≥12 mm (OR, 5.13 [95% CI, 1.38-19.1], P=0.015), and use of a bare metal stent (OR, 3.14 [95%, 1.37-7.20], P=0.007). Reinterventions: - 45 patients required catheter-based reinterventions (n=21 balloon angioplasty, n=24 stent implantation). - The cumulative incidence was 1.6% by immediate, 5.1% by early, and 21.3% by late follow-up. - Where data was available, reasons for intervention included staged re-expansion (n=5), aortic wall injury (n=11), restenosis (n=15). - Stent fractures were noted in 12 patients undergoing reintervention, only one with loss of structural integrity. - By multivariate analysis, independent predictors of reinterventions at late follow-up were: age <18 years (OR, 3.76 [95% CI, 1.10-12.9], P=0.035), coarctation minimum diameter <6mm (OR, 3.47 [95% CO, 1.21-9.98], P=0.021), minimum stent diameter at implantation <12 mm (OR, 4.16 [95% CI, 1.37-12.7], P=0.012); and post-implantation systolic arm-leg BP gradient ≥10 mm Hg (OR, 3.25 [95% CI, 1.13-9.35], P=0.029).

	Native Versus Recurrent Coarctation: - Study did not find significant differences of any outcome variable when comparing native, postsurgical, or postcatheterization coarctation. However, subtle differences in the need for reintervention and presence of aortic wall injuries are noted. - Reintervention incidence was 7% for postsurgical coarctation, 22% and 23% for native and postcatheterization. - Aortic wall injuries were not seen in the postsurgical group compared with 6 to 7% in native and postcatheterization coarctation.
Benefits/claims data	- At late follow-up, freedom from surgical intervention was 100%, catheter reintervention 78.7%, stent fracture 75.6%, and freedom from aortic wall injury 93.7%. - 44% of patients had suboptimal long-term hemodynamic outcomes. - It has documented that hemodynamic results are generally maintained over the follow-up period. Stent fractures, catheterization reinterventions, and aortic wall injuries, all increase in frequency between medium and long-term follow-up. Overed stents appear to confer some protection from the development of stent fractures, but they do not provide complete protection from late aneurysm formation.
Strengths	- The largest study to date with comprehensive follow-up data up to 60 months post-procedure.
Weaknesses/ Potential bias	- Small sample size - Did not have the statistical power to evaluate all parameters contributing to long-term morbidity in these patients, such as aortic wall injury. - Once the COAST studies were closed, it was not permissible to contact centers for additional data regarding stent fractures, indications for reintervention and other clinical data elements. - There were inherent differences between COAST and COAST II enrollment indications and the way some of the data was collected. - While this study defined 48 to 60 months follow-up as long-term, this is still a relatively short time period. - This study only analyzed the outcome of stent implantation for coarctation using CP stents. Ot did not compare the outcome of stent implantation to other treatment modalities, as was done in the Congenital Cardiovascular Interventional Study Consortium Report.[2]

State of the Art

Appraisal

Medical condition		Alternatives		Risk/benefit		Side-effects		Equivalence		Surrogate endpoints	
Yes 1	No 2	**Yes 1**	No 2	**Yes 1**	No 2	**Yes 1**	No 2	Yes 1	**No 2**	**Yes 1**	No 2

Overall SOA Appraisal and Disposition

SOA Grade (Range 6-12)	7	Disposition (select)	**Accepted, < 12** Excluded, 12

Relevant SOA Results

[2] Forbes TJ, Kim DW, Du W, Turner DR, Holzer R, Amin Z, Hijazi Z, Ghasemi A, Rome JJ, Nykanen D, Zahn E, Cowley C, Hoyer M, Waight D, Gruenstein D, Javois A, Foerster S, Kreutzer J, Sullivan N, Khan A, Owada C, Hagler D, Lim S, Canter J, Zellers T; CCISC Investigators. Comparison of surgical, stent, and balloon angioplasty treatment of native coarctation of the aorta: an observational study by the CCISC (Congenital Cardiovascular Interventional Study Consortium). J Am Coll Cardiol. 2011 Dec 13;58(25):2664-74. doi: 10.1016/j.jacc.2011.08.053. PMID: 22152954.

	SOA data	CoA: - CoA is repaired during the neonatal period and infancy by surgery. Beyond infancy, percutaneous treatment using either balloon angioplasty or stent implantation are more frequently employed to treat native or recurrent coarctation. - The Cheatham-Platinum (CP) Stent was developed by NuMED (Hopkinton, NY) specifically designed to treat aortic coarctation. It has rounded edges to reduce the incidence of aortic wall injury and can be expanded to 24mm diameter. - Stent implantation, balloon angioplasty, and surgery are all treatment options for coarctation in patients beyond infancy. - Treated coarctation is associated with long-term morbidity irrespective of treatment strategy. COAST Trials: - The FDA pivotal trials COAST (Coarctation of the Aorta Stent Trial; 2007-2016) demonstrated safety and efficacy of the bare CP Stent when used to treat aortic coarctation. Short- and medium-term results have been previously reported (Meadows et al. *(32)*). - The Covered CP Stent is a CP stent covered by a 0.28'' sleeve of 0.005'' thick expanded polytetrafluoroethylene tubing and was available to centers participating in the COAST trial for compassionate and emergency use for aortic wall injury occurring during aortic interventions.
	Comments	Hemodynamic Outcome: - Study corroborates the results from the largest multi-center study of stenting for coarctation from the Congenital Cardiovascular Interventional Study Consortium, which reported 23% systolic hypertension at 12 to 60 months of follow-up, 9% arm-leg blood pressure gradient ≥20 mm Hg, 23% need for antihypertensive medication and the presence of any of these 3 in 37%.[3] Stent Fractures: - Previous studies of the bare metal CP stent documented stent fractures of 2% at 12 months, and 12% at 24 months (Meadows et al. *(32)*). While the design and metallic composition of the CP stent may contribute, stents fractures are not limited to CP stents.[4] Boe et al.[5] reported a 21% fracture rate for Palmaz Genesis XD stents when used for coarctation therapy in children < 20Kg at a mean follow-up of 75 months. - It is unclear whether somatic growth can add additional force and loading conditions to the implanted stent, or whether participation in contact sports might impact the incidence of stent fractures. - Bare metal stents have a significantly higher fracture rate than covered CP stent. Possible explanations could be that the struts of a bare stent become more solidly embedded into the aortic wall, and that the expanded polytetrafluoroethylene covering more equally distributes the radial force to multiple struts or that it reduces the transmission of aortic pulsability to the struts. Reinterventions: - Previously reported data documented transcatheter reinterventions of about 5% by 24 months follow-up (Meadows et

[3] Holzer R, Qureshi S, Ghasemi A, Vincent J, Sievert H, Gruenstein D, Weber H, Alday L, Peirone A, Zellers T, Cheatham J, Slack M, Rome J. Stenting of aortic coarctation: acute, intermediate, and long-term results of a prospective multi-institutional registry--Congenital Cardiovascular Interventional Study Consortium (CCISC). Catheter Cardiovasc Interv. 2010 Oct 1;76(4):553-63. doi: 10.1002/ccd.22587. PMID: 20882661.

[4] McElhinney DB, Marshall AC, Schievano S. Fracture of cardiovascular stents in patients with congenital heart disease: theoretical and empirical considerations. Circ Cardiovasc Interv. 2013 Oct 1;6(5):575-85. doi: 10.1161/CIRCINTERVENTIONS.113.000148. PMID: 24129934.

[5] Boe BB, Loccoh E, Stockmaster K, Holzer RJ, Cheatham SL, Cheatham JP, Armstrong A, Berman DP. Median and long-term outcomes of stent implantation for coarctation of the aorta in small patients (<20 kg). [Abstract presented at PICS 2019]. *J Struct Heart Dis. 2018;4:140.*

		al. *(32)*). - There is no expert consensus defining when a reintervention should be performed. - Reinterventions in this patient population are not unexpected and do not represent a poor outcome. Aortic Wall Injury: - Aneurysms did not just occur in patients with bare metal stents, but equally in patients who had covered stents implanted. As such, the notion that covered stent implantation confers long-term protection from the development of aneurysm, may not be the case. Data are in contrast with Butera et al.[6] who did show a significant difference in the incidence of aneurysm formation when comparing patients bare versus covered stents, albeit in a much smaller cohort. Also, the median follow-up in that study was significantly longer for those with bare stents compared with covered stents (85 versus 35 months). This is important as the current study demonstrates that the majority of aneurysms were not identified until late follow-up. - Most aneurysms developed within the borders of the stent, including covered stents. One possible explanation is that pressure within the aorta distributes flow between the stent and the aortic wall, eventually leading to aneurysm formation. Another possibility is that the expanded polytetrafluoroethylene became damaged during initial implantation. - Current study did not investigate the benefit of a covered stent to reduce the risk of acute aortic wall injury during stent implantation because cases have not been randomly assigned and high-risk patients were excluded for bare stent implantation and received covered stents.

[6] Butera G, Manica JL, Marini D, Piazza L, Chessa M, Filho RI, Sarmento Leite RE, Carminati M. From bare to covered: 15-year single center experience and follow-up in trans-catheter stent implantation for aortic coarctation. Catheter Cardiovasc Interv. 2014 May 1;83(6):953-63. doi: 10.1002/ccd.25404. Epub 2014 Feb 4. PMID: 24459104.

An overall summary of the clinical performance and safety:

A comprehensive, systematic, and critical evaluation of the pertinent clinical data and pre-clinical study data in relation to the Bare Stents has been carried out and documented in the clinical evaluation report. Based on the results of that evaluation, it is considered that:

a) Conformity with relevant general safety and performance requirements set out in MDR Annex I under the normal conditions of the intended use of the device has been confirmed.
b) Undesirable side-effects and acceptability of the benefit-risk ratio have been evaluated and are acceptable according to the current knowledge/the state of the art in the medical fields concerned and according to available medical alternatives.
c) The information materials supplied by NuMED, and the risk reduction measures are adequate taking into account the intended purpose of the device.
d) Usability aspects have been adequately considered and the Stents, including the IFUs, are suitable for the intended users.
e) The claims foreseen in the information materials provided with the CER are adequate taking into account the intended purpose of the device.
f) The information materials supplied and the RM documentation for the device under evaluation are consistent with the clinical data and pre-clinical study data presented in the CER and with the current knowledge/state of the art.

Overall, it is concluded that the risks associated with the use of the Stents are acceptable when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety, taking into account the generally acknowledged state of the art; that the intended clinical performances are achieved by the device; and that known and foreseeable risks and undesirable side-effects are considered acceptable when weighed against the benefits from performance achieved by the device.

Ongoing planned post-market clinical follow-up:

The Stent Device Family has been on the market since 2004 in the EU and 1999 in other markets. Over time variants of the Stent Device Family have been introduced to these markets. Since then, the devices are likely to have been used in a variety of patients and populations. The Stents have been subjected to several clinical investigations where efficacy and safety has been demonstrated.

A PMCF study was not warranted at this time due to the fact that the long-term safety and clinical performance has been established via device use and ample clinical experience. This experience would likely have identified any rare complications or problems that would become apparent only after widespread device use. Continued PMS activities will provide sufficient data to adequately address clinical risks, and detect emerging risks on the basis of evidence. Additional clinical studies were conducted in the U.S. under the COAST and COAST II clinical trials.

A PMCF study was initiated in 2018 for the additional sizes that were added to the product line, to determine if there were any new complications which were previously not addressed through actual clinical use, or if any new risks are introduced. The target study size was 59 patients, based on a confidence level of 95%. The study was conducted by issuing a form to the treating physician and collecting data. The study is complete and the results are included in the clinical data that is used for the clinical evaluation.

6. Possible diagnostic or therapeutic alternatives

Alternative treatments for CoA include surgery or balloon angioplasty.

7. Suggested profile and training for users

The COA Stent Device Family is intended for use by a cardiac surgeon and/or interventionalist.

8. Reference to any harmonised standards and CS applied

There are no Common Specifications for this type of device.

The following harmonised standards are followed for this device:

- EN ISO 10993-10: 2023 – Biological Evaluation of Medical Devices – Part 10: Tests for Skin Sensitization
- EN ISO 10993-23: 2021 – Biological Evaluation of Medical Devices – Part 23: Tests for Irritation
- EN ISO 11135: 2014 / A1:2019 – Sterilization of health-care products – Ethylene oxide – Requirements for the development, validation and routine control of a sterilization process for medical devices.

- EN ISO 11737-1: 2018 / A1:2021 – Sterilization of medical devices – Microbiological methods – Part 1: Determination of a population of microorganisms on products
- EN ISO 13485: 2016 / A11:2021 – Medical devices – Quality management systems – Requirements for regulatory purposes
- EN ISO 14971: 2019 / A11:2021 – Medical Devices – Application of Risk Management to Medical Devices
- EN ISO 15223-1: 2021 – Medical devices – Symbols to be used with medical device labels, labelling and information to be supplied – Part 1: General requirements

9. References

1. Baykan A, Demiraldi AG, Tasci O, Pamukcu O, Sunkak S, Uzum K, Sezer S, Narin N, Is hypertension the fate of aortic coarctation patients treated with Cheatham Platinum (CP) stent? *Journal of Interventional Cardiology* **31**, 244-250 (2018).
2. Sohrabi B, Jamshidi P, Yaghoubi A, Habibzadeh A, Hashemi-Aghdam Y, Moin A, Kazemi B, Ghaffari S, Abdolahzadeh BM, Mahmoody K, Comparison between covered and bare Cheatham-Platinum stents for endovascular treatment of patients with native post-ductal aortic coarctation: immediate and intermediate-term results. *JACC. Cardiovascular interventions* **7(4)**, 416-423 (2014).
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10. Revision History

SSCP revision number	Date Issued	Change Description	Revision validated by Notified Body
00	21 June 2022	Initial implementation	☐ Yes Validation Language: English ☒ No
01	14 July 2023	Updated sections 4, 5, 7, 8, and 9 for CER Update.	☐ Yes Validation Language: English ☒ No

NuMED
Summary of Safety and Clinical Performance
SSCP – Stents - CoA

Document Revision: 01
Date issued: 14 July 2023

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 person. A more extensive summary of its safety and clinical performance prepared for healthcare professionals is found in the first part of this document.

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

1. Device identification and general information	
Device trade name(s)	CP Stent Mounted CP Stent
Manufacturer's name and address	NuMED, Inc. 2880 Main Street Hopkinton, NY 12965 USA
Year when first certificate (CE) was issued	2004
Basic UDI-DI	08877141600T2
2. Intended use of the device	
Intended purpose	The Stents are intended for implantation in the native and/or recurrent coarctation of the aorta. An aortic coarctation is a partial blockage or narrowing in the aorta, the body's main blood vessel distributing blood to all parts of the body. This blockage of the aorta makes the heart work harder to pump blood to your body and can weaken the heart muscle. Furthermore, this blockage can cause severe upper body hypertension (high blood pressure), increasing the risk of stroke. This blockage is present from birth.
Indications and intended patient groups	The device is used to treat any patients that have an aortic coarctation as long as none of the below listed contraindications and/or limitations are applicable.
Contraindications and/or limitations	The following patients should NOT receive the Stent: • Patients who are too small to allow the stent to pass through their arteries without damaging the artery; • Patients with a stiff aorta that does not get larger with balloon dilation. • Patients with blocked leg arteries making it difficult or unsafe to move the catheter and stent to the narrowed aorta; • Patients with any signs of infection; • Patients with active infection in the heart or blood vessels (endocarditis); • Patients with a known allergy to aspirin, other antiplatelet agents, or heparin; • Pregnancy.

3. Device description	
Description of the device	The Stents are balloon expandable and intended to permanently stay in your body. The Stents are used for coarctation of the aorta.

	The Stents are composed of heat-treated metal (90% platinum and 10% iridium) wire that is arranged in laser welded rows with a "zig" pattern. The number of rows determines the unexpanded length of the stent. The BIB Stent Placement Catheter is triaxial in construction with two lumens being used to inflate the balloon while one lumen is being used for tracking over a guidewire. The inner balloon is ½ of the outer balloon diameter and 1 cm shorter. The purpose of the double balloon catheter is to apply an incremental inflation for the purpose of dilating a stent. The inner balloon provides initial expansion of the stent and also acts as a tool to hold the stent on the catheter prior to the outer balloon being inflated. The outer balloon is then inflated, providing the remainder of the expansion. There are radiopaque platinum marker bands under the balloon shoulders, to aid during placement. The balloons are designed to inflate to the diameter and length listed on the label at a specific pressure. Thus, it is recommended that the device be used in conjunction with a mechanism to monitor pressure, an inflation device with pressure gauge.
Medicinal Substances	The Stents do not contain any medicinal substances.
Mode of Action	The Stents are implanted using a thin hollow tube (catheter) with a balloon on the end. Your physician will place the stent on the balloon at the start of your procedure. The catheter with the stent is then placed through the skin, typically into the artery in your upper leg. The balloon and stent are moved to the appropriate position at the narrowed part of your aorta. Once in place, the balloons are inflated to expand the stent. The catheter is then removed from the body and the stent stays in place.
Description of Accessories	All Stents are packaged and shipped to the physician with hemostasis valve tools. These tools are hollow tubes that are placed in the valve of the introducer to help the Stent move through that valve without any issues. The valve of the introducer is very tight to prevent blood loss during the procedure, so the tools help the Stent move through the valve without causing damage to the stent or moving the stent on the catheter.

4. Risks and Warning	
Contact your healthcare professional if you believe that you are experiencing side effects related to the device or its use or if you are concerned about risks. This document is not intended to replace a consultation with your healthcare professional if needed.	
How potential risks have been controlled or managed	The Stent Device Family has been developed in accordance with documented processes to ensure that it is designed, manufactured, packaged, and labelled in accordance with the current state of the art and meets all requirements of the appropriate regulations. Design verification activities were performed and include pre-clinical testing and clinical investigations. A clinical literature review has also been performed on the Stent Device Family. All risks identified during these activities were mitigated as far as possible and are considered acceptable in regards to the clinical benefit of the device. Continued review of all Post Market Surveillance and Post Market Clinical Follow-up Data is performed to identify any additional risks that may be identified after the device was placed on the market.
Remaining risks and undesirable effects	Cardiac catheterization and stent insertion carry certain risks. Potential complications & adverse effects associated with device use and indication include: • Femoral Artery Injury, Thrombosis or Psuedoaneurysm – injury or weakening of femoral artery, or development of a blood clot in femoral artery • Stent Migration – movement of the stent away from original implant site • Stent Stenosis – growth of tissue within the stent, leading to return of the blockage • Stent Fracture – break in the frame of the stent • Aortic Aneurysm/Pseudoaneurysm – weakening or injury of the aorta wall • Aortic Rupture/Tear – perforation or tearing of the aorta, causing internal bleeding • Stent Malposition – poor position of stent, requiring a 2nd stent • Hematoma - bruising at the site where the device is introduced into the body

	• Sepsis/infection - infection • Thrombosis/Thromboembolism - formation or presence of a blood clot • AV fistula formation - abnormal passageway between an artery and a vein • Transitory arrhythmia - irregular heartbeat • Endocarditis - infection within the stent • Bleeding - at the site of where the device is introduced into the body • Cell necrosis at the site of implant - death of cells at the implant site • Cerebrovascular Incident - stroke • Death
Warning and Precautions	The majority of warnings and precautions listed for the Stents pertain to the placement and use of the device in the cath. lab by the physician. MRI Conditional information is applicable to the Stents after they are implanted. This information should be used by any MRI technician that is performing an MRI procedure on any patient with a NuMED Stent implanted. All patients will be provided with an Implant Card after their procedure. This Implant Card will give the location of where to find the most up to date MRI parameters to be used for patients that have a NuMED Stent implanted.
Summary of any field safety corrective actions (FSCA including FSN) if applicable	Since commercialization, there has been one recall on the Bare CP Stent in 2003 (#Z-0983-03, completed in 2004) concerning the lack of PMA or 510(k) for the Bare CP Stent. The recall was conducted in the U.S. only. There have not been any Field Safety Corrective Actions or Field Safety Notices on any other version of the Stents.

5. Summary of clinical evaluation and post-market clinical follow-up	
Clinical background of the device	The NuMED Stent Device Family has been sold globally since 1999. The following data is based on the NuMED CP Stent®. It was tested and found to be safe and effective to widen the narrow part of the aorta related to coarctation of the aorta. A study was conducted with 105 patients weighing more than 77 lbs at the time of implant. Most patients (98%) were treated with one CP Stent®. On average arm systolic blood pressure was 27 mmHg higher than the leg pressure before the procedure. A reduction of a gradient to 15mmHg or less following the procedure suggests that the blockage is reduced effectively. By one month after bare metal stent placement the average leg pressure was 1 mmHg higher than the arm pressure. Two years after implant, 91% of patients had arm blood pressures less than 15 mmHg above their leg blood pressure which suggests that most of the treated aortas did not re-narrow. An overview of complications and additional treatments provided after the stenting procedure is shown below: • Serious complications related to the CP Stent® or implant procedure, such as: injury to the aortic wall and leg artery-vein fistula (an abnormal passageway between the artery and vein), were identified in 1 out of 20 (5%) patients within the first month of implant. • No patients needed surgery to repair the aorta, remove the stent or repair the arterial access site. • 1 out of 20 (5%) patients developed small aneurysms (weakened areas of the aorta) in the area of stent placement in the years following stent therapy, making CT or MRI imaging an important part of follow up care. However, none of the patients who developed aneurysms demonstrated symptoms or required surgery. All were successfully treated with covered stent placement. • Approximately 3 out of 20 (15%) patients required repeat cardiac catheterization for a

	second dilation of the stent, mostly to keep up with the size of the patient as he/she grew and for some to repair aortic wall injuries as noted above.
The clinical evidence for the CE marking	CE marking is based on data from two clinical studies, a review of published literature, and a review of post market surveillance data. Additional pre-clinical testing was performed as part of the development and design of the device. In vitro (on the bench) testing was performed on the devices as part of the Design History File. Biocompatibility testing was also performed on the materials used to manufacture this device to determine if it met the requirements for an implant in the human body. The device passed all tests.
Safety	The clinical data and pre-clinical study data demonstrated that the device performed as intended in the clinical setting; the device does not pose unacceptable safety concerns in the clinical setting; and any risks associated with clinical use of the device are acceptable when weighed against the benefits to the patient.

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.

Coarctation of the Aorta

Your cardiologist believes that relief of the blockage is important for your health and safety. There are three ways to relieve the blockage: by surgery, by stent implantation without surgery, or by balloon angioplasty.

Surgical Therapy

Surgical treatment of the blockage is usually performed through an incision on the side of the chest, approaching the aorta by spreading the ribs. The narrowed portion of the aorta is removed and then the aorta is sewn back together. For more complicated coarctation, surgery might be performed from the front of the chest, opening the breast bone and using heart lung bypass. For some patients a benefit of a surgical approach is that the repair can be performed without the use of man-made materials. However, for other (especially adult) patients a man-made tube graft or patch may be needed. Please consult with your surgeon regarding his or her approach. For younger patients, surgery results in a lower need for a second procedure to keep up with growth when compared to balloon or stent therapy.

Risks of surgery include: pain from the surgical incision, prolonged fluid drainage from the chest after surgery, chest or wound infection, longer recovery time compared to stent therapy, prolonged postoperative rib discomfort and increased risk of very high blood pressure occurring after immediately after surgery, requiring intravenous therapy in an ICU, compared to stent repair. There is a low risk, probably less than 5%, of developing an aneurysm (weakened areas of the aorta) in the area of surgery in the years following stent therapy, making CT or MRI imaging an important part of follow up care.

Stent Therapy (without surgery)

A stent is an expandable metal tube that is implanted into your aorta to keep it open. Surgery is not required for this procedure. The stent is implanted using a thin hollow tube (catheter) with a balloon on the end. The catheter with stent is inserted through the artery in the upper leg. The balloon and stent are then moved to the appropriate position to the narrowed part of your aorta. Once in place, the balloons are inflated to expand the stent against the aortic wall. The catheter is then removed from the body and the stent remains in place.

Balloon Angioplasty

A specially designed catheter with a tiny balloon is carefully guided through the artery to the blockage, then inflated to widen the opening and increase blood flow to the heart.

7. Suggested profile and training for users

The Stent Device Family is intended for use by cardiology and surgical professionals undertaking stent implantation.