NuMED
Summary of Safety and Clinical Performance
SSCP – Pulmonary PTV

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 PTV Family Tyshak Tyshak-X Tyshak II Tyshak Mini Tyshak NuCLEUS Z-MED-X Z-MED II-X COEfficient Mullins-X
Model Number	NuMED PTV Family – Model 1100 Tyshak – Model 102 Tyshak-X – Model 102X Tyshak II – Model 105 Tyshak Mini – Model 107 Tyshak NuCLEUS – Model 103 Z-MED-X – Model 302X Z-MED II-X – Model 305X COEfficient – Model 303 Mullins-X – Model 250.1X
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	08877141100S9
Medical device nomenclature description / text	EMDN – C019014 – CARDIAC VALULOPLASTY CATHETERS
Class of device	III
Year when first certificate (CE) was issued	1999

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	Recommended for Percutaneous Transluminal Valvuloplasty (PTV) of the pulmonary valve. • A patient with isolated pulmonary stenosis. • A patient with valvular pulmonary stenosis with other minor congenital heart disease that does not require surgical intervention.
Contraindications and/or limitations	There are no contraindications for this device. However, the success of the procedure is impacted by the patient's medical condition and its severity. Therefore, it is recommended that the device be carefully considered if it were to be used in patients with mild valvular stenosis and in patients with valvular stenosis with major congenital heart defects that require open heart surgery.

3. Device description	
Description of the device	The NuMED PTV Catheters are coaxial in construction. The inner and outer shafts are constructed of polyamide tubing. The x-line versions inner tubing is comprised of a multi-layer extrusion of polyamide that surrounds a braid of 304 LV Stainless Steel. All catheters feature a proximal end bifurcate with two distinct luminal passages. The inflation lumen terminates into a distally mounted balloon. This balloon is non-compliant. The balloon is 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 balloon size is ± 10 % at Nominal Pressure (NP) or Rated Burst Pressure (RBP) and the Rated Burst Pressure (RBP) is not to be exceeded. Catheters with NuCLEUS in the name feature a balloon with a waist. The balloon is designed with a waist formed into the middle of the balloon to allow accurate balloon placement and stability. Upon reaching a specified pressure, the waist will expand to the rated balloon diameter and dilate the valve to the rated diameter. The through lumen terminates at the tip of the catheter and will accept the passage of the appropriate guidewire. All catheter sizes will have radiopaque platinum marker band(s), centered or under the balloon shoulders to aid during placement. These devices are also designed to be used with an appropriately sized introducer and guidewire. The catheters are supplied sterile, by ethylene oxide gas, and are intended for single use only. The catheters are invasive and intended for transient use (continuous use of <60 minutes) on patients.

Reference to previous generation(s) or variants	N/A
Accessories which are intended to be used in combination with the device	There are no accessories that are intended to be used with this device.
Description of any other devices and products which are intended to be used in combination with the device	This device is designed to be used with a guidewire, introducer, and an inflation device with pressure gauge.

4. Risks and Warning	
Residual risks and undesirable effects	The clinical data, availability of guidelines from expert groups, established use of the device technology and the large numbers of devices sold demonstrate that there is high quality data of sufficient amounts to detect undesirable side-effects associated with the use of the PTV Catheters. Known and foreseeable clinical risks have been considered for the PTV Catheters in accordance with risk management (RM) procedure AP-346 and through the RM files for PTV Pulmonary Catheters and mitigated as far as possible (AFAP). Identified clinical residual risks/undesirable side-effects for the PTV Catheters are: Potential balloon separation following balloon rupture or abuse and the subsequent need to use a snare or other medical interventional techniques to retrieve the pieces. NOTE: There have been infrequent reports of larger diameter balloons bursting circumferentially, possibly due to the combination of tight focal strictures in large vessels. In <u>any</u> instance of a balloon rupture while in use, it is recommended that a sheath be placed over the ruptured balloon prior to withdrawal through the entry site. This can be accomplished by cutting off the proximal end of the catheter and slipping an appropriately sized sheath over the catheter into the entry site. For specific technique, refer to : tegtmeyer, Charles J., M.D. & Bezirdijan Diran R., M.D. “Removing the Stuck, Ruptured Angioplasty Balloon Catheter.” Radiology, Volume 139, 231-232, April 1981. Potential complications and related adverse effects associated with the valvuloplasty catheter use include, but are not limited to: - Perforation - Conduction System Injury - Thromboembolic Events - Cardiovascular Injury - Balloon Rupture - Arrythmia Development - Restenosis Development - Inflammation - Infection - Cardiac Tamponade

	- Valvular Regurgitation - Access Site Complications
Warning and Precautions	**Warnings** - CAUTION: 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. - Catheter balloon inflation diameter must be carefully considered in selecting a particular size for any patient. The inflated balloon diameter should not be significantly greater than valvular diameter. The choice of the balloon size to be used for valve stenosis has been established by the VACA Registry to be approximately 1.2 to 1.4 times the valve annulus. It is important to perform an angiogram prior to valvuloplasty to measure the size of the valve in the lateral projection. - Balloons ≥ 4cm in length may impinge upon the tricuspid mechanism and may injure it. - Balloons longer than 4cm are not recommended for children ≤ 10 years old. - Use only appropriate balloon inflation medium. Do not use air or gaseous medium to inflate the balloon. - 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. - 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. - The catheter should be used prior to the 'Use Before' date noted on the package label. - Right ventricular outflow tract damage has occurred with balloons larger than 1.5 times the size of valve annulus. - The catheter is intended for valvuloplasty applications only, and is not intended for angioplasty. - **THE CATHETER IS NOT INTENDED FOR USE WITH STENTS.** **Precautions** - Dilatation procedure 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 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. - 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. - Before removing the catheter from the sheath it is very important that the balloon is completely deflated. - Proper functioning of the catheter depends upon 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	There have been (3) FSCAs for devices in the Pulmonary PTV Family. All FSCAs were from the NuMED Canada, Inc. manufacturing location and were for labeling/IFU issues. One FSCA was in 2011, one was in 2021, and one was in 2022. No adverse events were reported for any of the FSCAs.

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

Summary of clinical data related to equivalent device:

NuMED has elected not to use the clinical data from an equivalent (clinical, technical, and biological characteristics) device(s). In the event there are devices considered equivalent, their data will be considered as similar devices.

Summary of clinical data from conducted investigations of the device :

1. **Study name:**

Purpose: To establish the safety and effectiveness of the Tyshak and Z-MED models of the NuMED PTV Catheters, utilized for pulmonary valvuloplasty.

Clinical Study Methodology: Prospective study of 130 subjects (100 patients for the Tyshak model and 30 patients for the Z-MED model).

Reference to the clinical study plan (and amendment) n°: IDE # G890030

Investigation Sites: Dr Hugh Allen, Children's Hospital of Columbus Dr Ziyad Hijazi, New England Medical Center Dr Thomas Jones, Children's Hospital and Medical Center Dr Larry Latson, The Cleveland Clinic Foundation Dr Robert Morrow, Arkansas Children's Hospital Dr Michael Kuhn, Loma Linda University Children's Hospital Dr Donald Hagler, The Mayo Clinic Foundation Dr John Moore, Dupont Children's Hospital Dr Daphne Hsu, Columbia-Presbyterian Medical Center Dr Paul Seib, Arkansas Children's Hospital Dr John Cheatham, Children's Hospital of Omaha	***Reference to Document n°: IDE # G890030***

Patient Population: Patients with >50mmHg gradient resting state or >35mmHg gradient resting state with right ventricular hypertrophy on ECG and/or echo.

Inclusion Criteria:

- Any patient with a pulmonary valve gradient of >50mmHg, resting state
- Any patient with a pulmonary valve gradient of >35mmHg, resting state with right ventricular hypertrophy on ECG and/or echo
- Patients with isolated pulmonary valve stenosis
- Patients with pulmonary valve stenosis with other minor congenital heart disease that does not require surgical intervention

Exclusion Criteria:

- Patients with pulmonary valve gradient of <35mmHg, with normal ECG
- Other significant cardiac abnormalities (such as tetralogy of Fallot, supravalve pulmonary stenosis, or infundibular pulmonary stenosis) where dilatation may be achieved but will not result in a significant change in the gradient and therefore be of no value to the patient
- Patients with pulmonary valvar stenosis with major congenital heart defects that require open heart surgery
- Patients enrolled in any other study for investigational devices or drugs should not be enrolled in this study.

Clinical Study Results:

Purpose	Criteria	Results
Procedural Success	Valvular pressure difference reduced by ≥ 50% or reduced to ≤ 30 mmHg.	97% success rate (n=103); No deaths

Devices Used: Tyshak indicated for patients with non-dysplastic valves and Z-MED indicated for patients with dysplastic and/or calcified valves.

Conclusion: The devices were found to be safe and effective for use in valvuloplasty.

Summary of clinical data from other sources:

The following is a summary of clinical data found during the literature review of the PTV Catheter Device Family:

Author	Results/Outcome
Yucel et al. 2016	**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)	11	Disposition (select)	**Accepted, < 12** Excluded, 12

Relevant Results: PS is defined as "severe" when the right ventricle pressure is equal to or greater than the systemic pressure. Patients with severe PS with duct-dependent pulmonary blood flow and/or signs and symptoms of low cardiac output are considered to have "critical pulmonary stenosis" (CPS).

Safety & Performance

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Retrospective review	To assess short- and midterm outcomes, and to describe the predictors of the need for additional pulmonary flow and reintervention after successful BVP	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	Tyshak II	**D1**	D2	D3
Application	BVP	**A1**	A2	A3
Patient	Neonates with severe PS Sampling: n=56 Median age: 7 days (2-28 days) Sex: Not Stated	**P1**	P2	P3
Report	High quality	**R1**	R2	R3
Suitability Grade (Range 4-12)		**4**		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	Procedural success	**Yes 1**	No 2
Follow-up	Median 57 months (2-119 months)	**Yes 1**	No 2
Statistical analysis	The quantitative data were expressed as the mean ± standard deviation and median range (maximum-minimum values. Independent samples T and Mann-Whitney U tests were used in the comparison of two independent groups. Wilcoxon signed-rank test was used for the comparison of TV with PV Z scores obtained prior to the procedure and at the end of the follow-up period. Odds ratio was used for determining the association between the presence of bipartite RV and the need for additional pulmonary blood flow or reintervention. Received operating curve (ROC) was applied to detect the significant predictors for patients who need additional pulmonary blood flow or reintervention. The data were analysed at 95% of confidence level and accepted as significant when the p value is lesser than 0.05.	**Yes 1**	No 2
Clinical significance	A successful BVP is a procedure in which a balloon catheter with an appropriate size can be placed across the valve, and a distinct waist in the balloon is eliminated with inflation.	**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 (4) + Data Contribution (4) = 12	Disposition and Weighting (select)	**Accepted and Pivotal 9-12** Accepted but not Pivotal, 13-21 Excluded, 22-25

Objective: Review of 56 neonates who underwent cardiac catheterization with the aim of BVP for CPS between 2005 and 2015 to assess short- and midterm outcomes, and to describe the predictors of the need for additional pulmonary flow and reintervention after a successful BPV.

Method: All echocardiographic, catheterization and angiographic data obtained prior to the initial BVP and at follow-up were reviewed for the following: pressure of the right ventricle (RV) and pulmonary artery (PA), tricuspid valve (TV) and pulmonary valve (PV) annulus diameter and Z score, pressure gradient across the PV and RV, PV morphology, presence and degree of tricuspid regurgitation, presence of subvalvar RVOT stenosis, presence of RV systolic dysfunction and patency of the AD. The TV and PV annulus diameters were obtained from four chamber and parasternal short axis views, respectively. The characteristics of the patients who needed pulmonary blood flow augmentation after a successful BVP were compared with those of the patients who did not need any further intervention.

Relevant Results:

Criteria	Results	P value

Procedure success rate	Successful in 55/56 (98%) patients. One unsuccessful case due to pulmonary valve not being crossed and patient required right ventricular outflow tract (RVOT) reconstruction.	NA
Mean balloon/annulus ratio	1.29 ± 0.12 (1.06–1.55)	NA
Oxygen saturation	Pre-procedural: 76 ± 9.3% increased to post-procedural: 89 ± 4.9%	P<0.001
Transvalvular peak-to-peak gradient	Pre-procedural: 76 ± 22 mmHg decreased to post-procedural: 10.6 ± 6.6 mmHg	P<0.001
Re-intervention	Transcatheter or surgical re-intervention was performed in 11 patients.	NA
Long term follow up	Of the 19 patients who underwent successful BPV, 13 (68 %) did not need any further intervention and are being followed up for a median of 72 months (11–119 months), with a median oxygen saturation of 96 % (89–99 %), whereas six (32 %) needed re-intervention.	NA

Safety concern:

Criteria	Results	P value
Adverse Events	Arrhythmia n=5, supraventricular tachycardia n=2, transient complete heart blocks n=2 and atrial flutter n=1. 2 patients suffered from a cold lower extremity as a result of mild femoral artery spasm after the procedure received overnight intravenous heparin. No thrombotic occlusion was observed. Mild PR was observed in 32 neonates, moderate in 9, and severe in 2.	NA

Conclusion: The study shows the excellent immediate outcomes of BPV in a pure cohort of patients with critical pulmonary stenosis. The need for additional pulmonary blood flow after a successful BPV is not rare.
Device used: Tyshak II

Al Balushi et al. 2013

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)	9	Disposition (select)	**Accepted, < 12** Excluded, 12

Safety & Performance
Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Retrospective review	To characterise the status of pulmonary regurgitation on follow up after pulmonary valve balloon dilatation (PVBD).	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	Tyshak 2 and Z-Meditech	**D1**	D2	D3
Application	PVBD	**A1**	A2	A3
Patient	Consecutive patients with isolated pulmonary valve stenosis Sampling: n=50 Mean age: 2.23 years (range: 2 days – 18 years) Sex: 32 M; 18 F	**P1**	P2	P3
Report	High quality	**R1**	R2	R3
Suitability Grade (Range 4-12)		**4**		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	Rate and degree of pulmonary valve regurgitation	**Yes 1**	No 2
Follow-up	Mean: 4 years (range: 2-6 years)	**Yes 1**	No 2
Statistical analysis	Mean standard deviation and ranges were calculated for continuous variables. Frequencies were determined for nominal and ordinal variables. Univariate and multivariate logistic regression analyses were used to examine the risk factors for the development of moderate and severe pulmonary valve regurgitation that included age, balloon to annulus ratio, and valve morphology. A P< 0.05 was considered to be statistically significant.	Yes 1	**No 2**
Clinical significance	Doppler echocardiography was used at the last follow-up to assess the degree of pulmonary valve regurgitation as mild when the diastolic flow reversed midway between the valve and the bifurcation of the pulmonary trunk, as moderate when the reversal reached the level of the bifurcation, and as severe when flow reversal was seen within branch pulmonary arteries.	**Yes 1**	No 2
Data Contribution Grade (Range 4-8)		**5**	

Overall S&P Appraisal, Disposition and Weighting

S&P Grade	LOE (4) + Suitability (4) +	Disposition and Weighting (select)	Accepted and Pivotal 9-12

(Range 9-25)	**Data Contribution (5) = 13**		**Accepted but not Pivotal, 13-21** Excluded, 22-25

Objective: Characterizes the status of pulmonary regurgitation on follow up after pulmonary valve balloon dilatation and to study the determinant of the severity of PR.
Method: Review of 50 consecutive patients undergoing pulmonary valve balloon dilatation in 2004 – 2009 and were assessed with follow-up Doppler echocardiography. The impact of balloon to annulus ratio, age, and valve anatomy on the late development of moderate and severe pulmonary valve regurgitation following balloon valvuloplasty was analysed.

Relevant Results:

Criteria	Results	P value
Peak right and left ventricle systolic pressure	Mean pre-dilatation right ventricle – 90 mm Hg and left ventricle – 78 mm Hg. Mean post-dilatation right ventricle – 47 mmHg and left ventricle – 81 mm Hg.	NA
Mean balloon to annulus ratio	1.4 (range: 1 – 1.66)	NA

Safety concern:

Criteria	Results	P value
Adverse Events	No pulmonary valve regurgitation in 6 patients (12%), mild pulmonary valve regurgitation in 32 patients (64%), moderate pulmonary valve regurgitation in 9 patients (18%) and severe pulmonary valve regurgitation in 3 patients (6%).	NA

Conclusion: Pulmonary valve regurgitation is a common finding in midterm follow-up after balloon valvuloplasty and the majority of patients have mild pulmonary regurgitation. Moderate to severe pulmonary regurgitation is well tolerated at midterm follow-up and perhaps not related to age, balloon size, or valve anatomy.
Device used: Tyshak II and Z-Meditech balloons

Behjati-Ardakani et al. 2013

Safety & Performance
Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Prospective study	To evaluate the long term results of balloon pulmonary valvuloplasty	1	2	**3**	4	5

Suitability	Relevant Data	Grading		
Device	Tyshak	**D1**	D2	D3
Application	PBPV	**A1**	A2	A3
Patient	Patients with moderate to severe valvular pulmonary stenosis Sampling: n=98 Median age: 6.75 years (range: 0.4 to 52 years) Sex: 50 M; 48 F	**P1**	P2	P3
Report	High quality	**R1**	R2	R3
Suitability Grade (Range 4-12)		**4**		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	Peak to peak pressure gradient across pulmonary valve & Peak instantaneous gradient across the pulmonary valve	**Yes 1**	No 2
Follow-up	Median: 4.1 years (Range 2 to 13.5 years)	**Yes 1**	No 2
Statistical analysis	Normally distributed continuous variables were expressed as mean ± SD. When the data are not normally distributed, medians (range) are given. Mean pressure gradients before and immediately after BPV and at short, intermediate and long-term follow up were compared by two tailed or paired student's t-tests. A P-value less than 0.05 was considered statistically significant.	**Yes 1**	No 2
Clinical significance	Peak to peak pressure gradient reduction >30 mmHg	**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) = 12**	**Disposition and Weighting (select)**	**Accepted and Pivotal 9-12** Accepted but not Pivotal, 13-21 Excluded, 22-25

Objective: Describes the results of long-term follow up of BPV in 96 patients with congenital pulmonary valve stenosis.
Method: From June 1998 to January 2012, percutaneous balloon pulmonary valvuloplasty for congenital pulmonary valve stenosis was performed in 98 patients (50 males, 48 females, with a median age of 6.75 years) underwent balloon valvuloplasty of pulmonary valve stenosis. Follow-up was performed based on the Doppler echocardiographic data and clinical findings.
Relevant Results:

Criteria	Results	P value
Peak to peak pressure gradient across pulmonary valve	Pre BPV: 88.7 ± 36.4 mmHg (range 52-195 mmHg) Post BPV: 21.8 ± 15.9 mmHg (range 0-100 mmHg)	NA
Peak instantaneous gradient across	Pre BPV: 93.2 ± 14.3 mmHg (range 52-202 mmHg)	P<0.001

	the pulmonary valve	At 3 months: 18.7 ± 15.8 mmHg (range 0-85 mmHg) At 1 year: 15.8 ± 13.1 mmHg (range 0-65 mmHg) Long term follow up: 13.6 ± 7.4 mmHg (range 0-33 mmHg)	P<0.001 P<0.001 P<0.017

Safety concern:

Criteria	Results	P value
Adverse Events	Mild pulmonary regurgitation was observed in 55 (57%) patients, immediately after BPV, 40 (43%) patients at short, 30 (31%) at intermediate and 30 (31%) at long term follow up. Moderate pulmonary regurgitation was noted in two (2.1%) patients immediately after BPV. Moderate PR did not regress at long-term follow up. On short and intermediate follow- up three patients required a second balloon dilatation with excellent results. None of patients had significant pulmonary regurgitation at long term follow up. Perforation of right ventricular outflow tract (RVOT) was the major complication in two (2%) patients with fatal event. This complication is rare and usually occurs in patients with annular hypoplasia and fixed infundibular pulmonary stenosis	NA

Conclusion: In conclusion, the results of BPV have been so successful that in recent year it has large replaced surgical valvotomy except in patients with dysplastic pulmonary valves and fixed (non-functional) infundibular stenosis. It is a nonsurgical procedure and is associated with shorter hospital stays, less psychological discomfort and avoiding scar. Although in our study result of balloon valvuloplasty, immediately after balloon valvuloplasty was not acceptable, but the short, intermediate and long-term results were excellent. There BPV can be considered as the treatment of choice for patients with typical valvular pulmonary stenosis and cases with annular hypoplasia and fixed infundibular stenosis should be referred to cardiovascular surgeon.
Device used: Tyshak

Maostafa et al. 2013

Safety & Performance
Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Prospective study	To evaluate the results of long term follow up of BPV in 60 children	1	2	**3**	4	5

Suitability	Relevant Data	Grading		
Device	Tyshak	**D1**	D2	D3
Application	BPV	**A1**	A2	A3
Patient	Patients with moderate to severe valvar pulmonary stenosis Sampling: n=53 Mean age: 3.2 years (range: 0.4 – 8 years) Sex: 25 M; 28 F	**P1**	P2	P3
Report	High quality	**R1**	R2	R3
Suitability Grade (Range 4-12)		**4**		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	Peak-to-peak systolic pressure gradient across the pulmonary valve Maximum peak instantaneous Doppler pressure gradient Re-stenosis	**Yes 1**	No 2
Follow-up	Median: 5.5 years (Range: 2 to 13.5 years)	**Yes 1**	No 2
Statistical analysis	Normally distributed continuous variables were expressed as mean ± standard deviation (SD). Pressure gradients before and immediately after balloon valvuloplasty and at long-term follow-up were compared by two tailed or paired t-tests. A P-value <0.05 was considered statistically significant.	**Yes 1**	No 2
Clinical significance	Gradient < 30 mmHg	**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) = 12	Disposition and Weighting (select)	Accepted and Pivotal 9-12 Accepted but not Pivotal, 13-21 Excluded, 22-25

Objective: Reports long term results of 2–13. 5 years follow up of balloon pulmonary valvuloplasty in children.
Method: Right ventricular to pulmonary artery pressure gradient was measured pre and immediately post– valvuloplasty at catheterization, and then by echocardiography at follow up. Follow up studies were performed 2–13.5 years after procedure, by Doppler echocardiography in all patients and catheterization and angiography in two patients.
Relevant Results:

Criteria	Results	P value
Peak–to–peak systolic pressure gradient across the pulmonary valve	Reduced from 83.28±32 (range: 55–170 mmHg) before BPV to 19.3±14.2 (range: 0–75 mmHg) immediately after BPV. At short term follow-up (≤ 3 months), 15.1±9.5 mmHg) (range: 0-48	P<0.005 P<0.001

	mmHg).	
Maximum peak instantaneous Doppler pressure gradient	Declined from 15.1±9.5 at short term (≤ 3 months) to 13.02±703 (range 0-36 mmHg at intermediate- term (> 3 months < 1 year) And further declined to 12.3±6.6 mmHg (range: 0- 32) at long-term follow up	P<0.001 P<0.001 (compared to short term results)
Re-stenosis	2/53 patients had re-stenosis (defined as a pressure gradient 50 mmHg or more) at intermediate- term follow up.	NA

Safety concern:

Criteria	Results	P value
Adverse Events	There was one immediate death because of cardiac tamponade following rupture of right ventricular outflow tract. Pulmonary regurgitation was absent in 33 (62.2%) cases, mild in 18 (34%) and moderate in 2 (3.8%) at short–term follow up. Incidence of pulmonary regurgitation by Doppler echocardiography was lower at follow up, 20 (38%) cases at short–term versus 17 (32%) cases at long–term).	NA P<0.001

Conclusion: The study shows balloon valvuloplasty is a safe and effective treatment of moderate and severe pulmonary valve stenosis. The short, intermediate and long- term results in children are excellent.
Device used: Tyshak balloon catheter

Santamaria et al. 2015

Safety & Performance
Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Retrospective review	To report experience with palliative oulmonary valvuloplasty in the management of children with unrestrictive VSD or single ventricle associated with severe PS focusing on procedural efficacy and clinical outcomes	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	Boston Scientific Sterling, Braun Medical Tyshak or Boston Scientific Symmetry	**D1**	D2	D3
Application	Pulmonary valvuloplasty	A1	**A2**	A3
Patient	Patients with severe pulmonary stenosis associated with unrestrictive ventricular septal defect or a form of single ventricle heart disease who underwent palliative pulmonary valvuloplasty Sampling: n=16; n=7 treated with a Tyshak balloon catheter Mean age: 25 days (range: 1-352 days) Sex: not Stated	**P1**	P2	P3
Report	High quality	**R1**	R2	R3
Suitability Grade (Range 4-12)		**5**		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	Primary efficacy endpoint: improvement in antegrade pulmonary blood flow assessed as the increase in oxygen saturation after valvuloplasty Secondary endpoints: change in Qp:Qs and PA pressure Longer-term clinical endpoints: time, oxygen saturation and weight gain	**Yes 1**	No 2
Follow-up	4 months	**Yes 1**	No 2
Statistical analysis	Baseline and demographic characteristics were summarized by standard descriptive statistics using mean with standard deviation for normally distributed continuous variables, median with range for skewed continuous variables, and count or proportion for categorical variables. Assessments of differences in primary and secondary endpoints before and after intervention were tested using paired t-test or Wilcoxon signed rank. Statistically significance was established at P<0.05.	**Yes 1**	No 2
Clinical significance	Significant increase in pulmonary blood flow and systemic arterial oxygen saturation.	**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) = 12	Disposition and Weighting (select)	Accepted and Pivotal 9-12 Accepted but not Pivotal, 13-21 Excluded, 22-25

Objective: Review of experience with palliative pulmonary valvuloplasty in the management of children with unrestrictive ventricular septal defect or single ventricle associated with severe pulmonary stenosis focusing on procedural efficacy and clinical outcomes.
Method: Retrospective review of all patients with severe pulmonary stenosis associated with unrestrictive ventricular septal defect or single ventricle who underwent palliative pulmonary valvuloplasty as initial management and describe outcomes. The primary efficacy endpoint was the improvement in the antegrade pulmonary blood flow assessed as the increase in oxygen saturation after valvuloplasty.

The secondary end points were the change in QP:QS and
PA pressure. Additionally, longer-term clinical endpoints including time, oxygen saturation, and weight gain before next intervention aimed to increase pulmonary flow were reviewed.

Relevant Results:

Criteria	Results	P value
Right ventricle pressure	Pre-intervention: 76±14 mm Hg and post-intervention: 73±15 mmHg	P = 0.9
PA Systolic pressure	Pre-intervention: 17.1±4.4 mm Hg and post-intervention: 26.3±7.8 mmHg	P = 0.007
PA Diastolic pressure	Pre-intervention: 9.2±3.4 mm Hg and post-intervention: 11.6±5.2 mmHg	P = 0.37
PA mean pressure	Pre-intervention: 11.7±3.7 mm Hg and post-intervention: 16.6±5.1 mmHg	P = 0.02
RVOT gradient	Pre-intervention: 61.1±12.7 mm Hg and post-intervention: 37.1±11.1 mmHg	P = 0.01
Systemic arterial O_2 saturation	Pre-intervention: 74.7±8.7 % and post-intervention: 83.1±8.8 %	P = 0.008

Safety concern:

Criteria	Results	P value
Adverse Events	Procedural complications included 3 cases of transient junctional ectopic tachycardia without hemodynamic changes (n=1) and lower extremity arterial thrombosis that were treated successfully with heparin (n=2). In the 14 patients who had post procedural echocardiographic imaging, only one patient had severe pulmonary insufficiency while all others had mild or less pulmonary insufficiency during the follow-up period.	NA

Conclusion: Balloon pulmonary valvuloplasty may be an appropriate alternative palliative therapy for select cyanotic patients with large unrestrictive ventricular septal defect or single ventricle associated with severe pulmonary stenosis who are deemed high risk for surgical palliation. It can provide a durable increase in oxygen saturation and allow time for weight gain before definitive therapy and may avoid complications related to surgical palliative shunting such as pulmonary hypertension, shunt failure, and anatomic alteration of pulmonary arteries.

Device used: Tyshak

Moguillansky et al. 2010

Safety & Performance

Appraisal

Level of Evidence	Study Method/Design	Question Applied	Oxford LOE 2011				
	Retrospective review	To evaluate initial success rates and freedom from intervention	1	2	3	**4**	5

Suitability	Relevant Data	Grading		
Device	**Tyshak II (Numed), Symmetry (Boston Scientific), Zmed II (Numed) and XXL (Boston Scientific)**	**D1**	D2	D3
Application	**PVBV**	**A1**	A2	A3
Patient	**Patients undergoing BPV for isolated severe pulmonary valve stenosis** **Sampling: n=35** **Age: <3 years** **Sex: Not Stated**	**P1**	P2	P3
Report	**High quality**	**R1**	R2	R3
Suitability Grade (Range 4-12)		**4**		

Data Contribution	Relevant Data	Grading	
Outcomes/Endpoints	Procedural success	**Yes 1**	No 2
Follow-up	Median: 27 months (IQR 14-38 months)	**Yes 1**	No 2
Statistical analysis	Continuous variables were expressed as medians and interquartile ranges (IQR) using Mann-Whitney test for independent variables and Wilcoxon matched-pairs signed-rank test for correlated variables. Categorical variables were analyzed with Fisher's exact test and expressed as percentages. Two-sided P values of <.05 were considered significant.	**Yes 1**	No 2
Clinical significance	Procedural success was defined as a post BPV gradient < 30 mmHg and freedom from re-intervention	**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 (4) + Data Contribution (4) = 12	Disposition and Weighting (select)	Accepted and Pivotal 9-12 Accepted but not Pivotal, 13-21 Excluded, 22-25

Objective: Reviews all cases of isolated PS in patients < 3 years undergoing BPV.

Method: Patients who responded to initial low pressure BAV (defined as inflation pressure <8 atmospheres) were followed in the LP-PVBV group, and those who failed low pressure BAV and required high pressure BAV (inflation pressure >8 atmospheres) were followed in the HP-PVBV group. Study outcomes were initial success rate (gradient post BPV < 30 mm Hg) and freedom from re-intervention. Possible predictors of failure to low pressure BPV were explored (age, hemodynamic data, pulmonary valve leaflet

maximal thickness, diameter/z-scores for pulmonary valve annulus, sinotubular junction, and subvalvar area).

Relevant Results:

Criteria	Results	P value
Procedural success (gradient post BPV < 30mm Hg and freedom from re-intervention)	N=27 (77.1%) successfully underwent low pressure BPV, n=8 successfully underwent high pressure BPV after failing low pressure BPV.	NA
Pulmonary valve gradient	Significant decrease in gradient in LP-PVBV group with median gradient 17 mmHg	P<0.001
	Significant decrease in gradient in HP-PVBV group with median gradient 21.5 mmHg	P=0.01
Long term follow up	Pulmonary insufficiency was trace-mild n=14, mild – moderate n=4, moderate n=3 in LP-PVBV group and trivial-mild n=5, moderate n=1 in HP-PVBV group. Age and maximal pulmonary valve thickness found to be predictors of failure of low pressure BPV.	NA

Safety concern:

Criteria	Results	P value
Adverse Events	Transient arrhythmia n=5 (14%), retroperitoneal hematoma n=1	NA

Conclusion: High pressure BPV can be performed safely in patients with isolated PS that fail low pressure BAV, with high success rate and acceptable long-term results. Failure to low pressure BAV is difficult to predict and authors continue to recommend that low pressure balloons as the first line of therapy.

Device used: Tyshak II and Z-MED II used for low profile and low pressure group. Z-MED used in high pressure group.

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 PTV Catheters has been carried out and documented in the CER. Based on the results of this 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, 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 PTV Catheters, including the IFU, is 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 PTV Catheters 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 PTV Catheters have been commercialized since 1999 in the EU. Since then, the device is likely to have been used in a variety of patients and populations. A PMCF study is not warranted at this time due to the fact that 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 post-market surveillance activities will provide sufficient data to adequately address clinical risks, and detect emerging risks on the basis of evidence.

NuMED has implemented a PMCF for the Tyshak NuCLEUS, which was added in 2013, to follow up on the safety, effectiveness and performance of the Tyshak NuCLEUS. The study population includes patients exposed to the Tyshak NuCLEUS Catheter. Data will be collected by means of a form/questionnaire that will be disseminated to distributors and users. The objective of the PMCF plan is to determine if there is an increase in complications and/or complaints with the Tyshak NuCLEUS as compared to other PTV configurations. All PMCF forms and sales and complaint data will be reviewed on a monthly basis.

Post-market surveillance data as part of the quality system is continually compiled as per an established quality system. Device-related adverse events and complaints are recorded with explicit purpose to identify and investigate any residual risks associated with the use of the device.

6. Possible diagnostic or therapeutic alternatives

Alternative treatments for valvular stenosis include metallic commissurotomy, surgical valvotomy and valve replacement, either transcatheter or surgical. Complications associated with these alternative treatments are the same as those for balloon valvuloplasty. In addition, disability and cognitive deficit were identified as potential complications for SAVR but were not identified for any of the other alternative treatment modalities.

7. Suggested profile and training for users

The intended users of PTV catheters are Cardiac Surgeons and/or Interventionalists.

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 11135:2014 – 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 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. Yucel, I.K., et al., *Intervention in Patients with Critical Pulmonary Stenosis in the Ductal Stenting Era.* Pediatric Cardiology, 2016. **37**(6): p. 1037-1045.
2. Al Balushi, A.Y., et al., *Pulmonary valve regurgitation following balloon valvuloplasty for pulmonary valve stenosis: Single center experience.* Annals of Pediatric Cardiology, 2013. **6**(2): p. 141-144.
3. Behjati-Ardakani, M., et al., *Immediate, short, intermediate and long-term results of balloon valvuloplasty in congenital pulmonary valve stenosis.* Acta Medica Iranica, 2013. **51**(5): p. 324-328.
4. Maostafa, B.A., M. Seyed-Hossien, and R. Shahrokh, *Long-term results of balloon pulmonary valvuloplasty in children with congenital pulmonary valve stenosis.* Iranian Journal of Pediatrics, 2013. **23**(1): p. 32-36.
5. Santamaria, R.W.L., et al., *Palliative balloon pulmonary valvuloplasty for infants with unrestrictive ventricular septal defect or single ventricle associated with severe pulmonary stenosis.* Catheterization and Cardiovascular Interventions, 2015. **86**(5): p. 829-833.
6. Moguillansky D, S.H., Rome JJ, Kreutzer J. , *Role of high-pressure balloon valvotomy for resistant pulmonary valve stenosis.* Congenit Heart Dis. , 2010. **5**(2): p. 134 - 40.

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