COBRA PzF NCS

NanoCoated Coronary Stent System

Instructions for Use

CAUTION: Federal law restricts this device to sale by or on the order of a physician

STERILE — DO NOT RESTERILIZE — SINGLE USE ONLY.

DO NOT USE IF STERILE PACKAGE IS OPENED OR DAMAGED.

The components of the COBRA PzF NanoCoated Coronary Stent System are STERILE.

Caution: Federal Law (USA) restricts this device to sale by or on the order of a physician.

This device is supplied in sterile condition. All materials inside the sterile barrier pouch (the delivery system and stent, as well as the carrier tube and pouch liner) are sterile. The external surface of the sterile barrier pouch, as well as the product carton, should not be considered sterile.

The COBRA PzF NanoCoated Coronary Stent System is not made with natural rubber latex.

1.0 PRODUCT DESCRIPTION

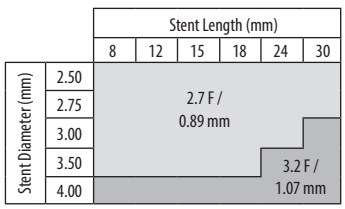
CeloNova's COBRA PzF NanoCoated Coronary Stent System is comprised of two main components: a premounted cobalt chromium (CoCr) alloy stent that is coated with Polyzene-F nanocoating and a balloon expandable delivery system. The COBRA PzF NanoCoated stent (NCS) is available in a Rapid Exchange (RX) system configuration. The system includes the following sizes:

Stent Diameter (mm)	Stent Length (mm)	Reference Vessel Diameter [RVD] (mm)	Lesion Length (mm)
2.50, 2.75, 3.00, 3.50, 4.00	8, 12, 15, 18, 24, 30	≥ 2.5 and ≤ 4.0	≤ 24

1.1 Device Component Description

The device component characteristics are summarized in Table 1.1-1.

Table 1.1-1: Device Component Description

	COBRA PzF NanoCoated Coronary Stent System
Available Stent Lengths (mm)	8, 12, 15, 18, 24, 30
Available Stent Diameters (mm)	2.50, 2.75, 3.00, 3.50, 4.00
Stent Material	An L-605 cobalt chromium CoCr alloy (including its major elemental constituents cobalt, chromium, tungsten, and/or nickel)
Polymer NanoCoating Description	An inorganic high molecular weight polymer [Poly-bis(trifluoroethoxy) phosphazene] ultrathin, durable, highly purified and flexible
Delivery System Working Length	135 cm
Delivery System Design	RX: Single access port to inflation lumen; guide wire exit notch is located 23-35 cm from tip; designed for guide wires ≤ 0.014 "
Stent Delivery System Balloon	A compliant, tapered balloon with two radiopaque markers located on the catheter shaft to indicate balloon and stent positioning
Minimum Guiding Catheter Inner Diameter	≥ 5F / 0.056" / 1.42 mm
Catheter Shaft Outer Diameter	
Percent Stent Free Area	82 – 86%
Balloon Deployment Pressure (2.50, 2.75, 3.00, 3.50, 4.00mm)	Nominal Pressure: 10 ATM (1013 kpa) Rated Burst Pressure (RBP): 16 ATM (1621 kpa)
Balloon Deflation Times	2.50 – 3.50 Diameter Balloons: ≤ 15 sec 4.0 Diameter Balloons: ≤ 20 sec
Hydrophilic coating	Hydrophilic coating has been applied to the delivery system, between the guide wire notch and the proximal balloon bond.

CELO NOVA BIOSCIENCES

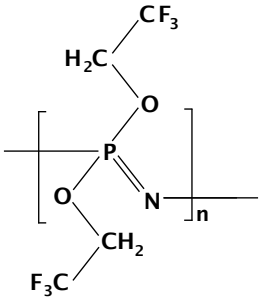
1.2 Polyzene-F NanoCoating Description

The COBRA PzF stent is coated with Polyzene-F nanocoating.

1.2.1 Polyzene-F

An inorganic high molecular weight polymer [Poly-bis(trifluoroethoxy)phosphazene] nanothin, durable, highly purified and flexible.

Figure 1.2.1-1 Polyphosphazene (PzF) Chemical Structure



1.3 Product Matrix

Table 1.3-1 COBRA PzF NanoCoated Coronary Stent System Product Matrix

Nominal Unexpanded Stent Length (mm)	Nominal Expanded Stent Diameter (mm)	REF Number
8	2.50	170-03-25008
	2.75	170-03-27508
	3.00	170-03-30008
	3.50	170-03-35008
	4.00	170-03-40008
12	2.50	170-03-25012
	2.75	170-03-27512
	3.00	170-03-30012
	3.50	170-03-35012
	4.00	170-03-40012
15	2.50	170-03-25015
	2.75	170-03-27515
	3.00	170-03-30015
	3.50	170-01-35015
	4.00	170-03-40015
18	2.50	170-03-25018
	2.75	170-03-27518
	3.00	170-03-30018
	3.50	170-03-35018
	4.00	170-03-40018
24	2.50	170-03-25024
	2.75	170-03-27524
	3.00	170-03-30024
	3.50	170-03-35024
	4.00	170-03-40024
30	2.50	170-03-25030
	2.75	170-03-27530
	3.00	170-03-30030
	3.50	170-03-35030
	4.00	170-03-40030

2.0 HOW SUPPLIED

- Sterile - This device is sterilized with ethylene oxide gas. Do not use if the sterile package is opened or damaged. Do not resterilize.
- Contents - One (1) COBRA PzF NanoCoated stent pre-mounted on a balloon expandable delivery system.
- Storage - Store in a dry, dark, cool place. Do not remove from carton until ready for use.

3.0 INDICATIONS FOR USE

The COBRA PzF NanoCoated Coronary Stent System is indicated for improving coronary luminal diameter in patients, including patients with diabetes mellitus, with symptomatic ischemic heart disease due to de novo lesions in native coronary arteries. The COBRA PzF NanoCoated stent is intended for use in patients eligible for percutaneous transluminal coronary angioplasty (PTCA) with reference vessel diameter (RVD) of 2.5-4.0mm and lesion length of ≤24mm.

Stent Diameter (mm)	Stent Length (mm)	Reference Vessel Diameter (mm)	Lesion Length (mm)
2.50, 2.75, 3.00, 3.50, 4.00	8, 12, 15, 18, 24, 30	≥ 2.5 and ≤ 4.0	≤ 24

4.0 CONTRAINDICATIONS

The COBRA PzF NanoCoated Coronary Stent System is contraindicated for use in patients with:

- known sensitivity to L605 cobalt-chromium alloy (including its major elemental constituents cobalt, chromium, tungsten, and/or nickel).
- contraindication to coronary artery stenting:
  - Patients with lesions that may prevent complete inflation of an angioplasty balloon, proper placement of the delivery device or stent deployment;
  - Patients are unable to receive recommended anti-platelet and/or anti-coagulant therapy.
- known severe reaction to contrast agents that cannot be adequately pre-medicated prior to the COBRA PzF NanoCoated Coronary Stent System placement procedure.

5.0 WARNINGS

- Contents supplied sterile using an ethylene oxide (EO) process. Do not use if sterile barrier has been opened or is damaged prior to use.
- This device is intended for single use only. Do not re-sterilize and/or reuse as this can potentially result in increased risk of inadequate sterilization, cross contamination and compromised device performance.
- Use of this device carries the associated risks of stent thrombosis, vascular complications, and bleeding events. Judicious patient selection and administration of appropriate anticoagulant and anti-platelet therapy are necessary to reduce these risks.
- When more than one stent is required, resulting in stent-to-stent contact, stent materials should be of similar composition to avoid the possibility of corrosion due to the presence of dissimilar metals in a conducting medium. The PzF SHIELD trial specified that lesions were to be covered with one stent of adequate length. For bailout procedures or in the event of sub-optimal results, further stenting using the COBRA PzF Coronary Stent was left to investigator's discretion.

6.0 PRECAUTIONS

6.1 Precautions: General

The risks and benefits of treatment with a coronary stent should be considered before using the COBRA PzF NanoCoated Coronary Stent System.

- Only physicians who have received adequate training in stent placement should perform implantation of this device.
- Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery can readily be performed.
- Do not use if labeling is incomplete or illegible.
- The delivery system must not be exposed to organic solvents (e.g., alcohol or detergents).
- Methods for safely treating in-stent restenosis of a COBRA PzF NanoCoated Stent (e.g., use of atherectomy devices or laser angioplasty catheters) have not been evaluated.
- Subsequent development of in-stent restenosis may necessitate repeated dilatation within the arterial segment. Data regarding the outcome of repeated dilatation within re-endothelialized COBRA PzF NanoCoated Stents are not available.

- Compared to use within the specified Indications for Use, the use of COBRA PzF NanoCoated stents in patients and lesions outside the labeled indications, including more tortuous anatomy, may have an increased risk of adverse events, including stent thrombosis, stent embolization, MI, or death.

6.2 Precautions: Pre- and Post-Procedure Antiplatelet Regimen

- Appropriate anticoagulant/anti-platelet therapy should be administered according to current medical guidelines. For reference, the 2016 ACC/AHA Guidelines are provided at the following website: http://dx.doi.org/10.1016/j.jacc.2016.03.513.
- In the PzF SHIELD trial, the protocol recommended aspirin indefinitely and recommended Clopidogrel, Prasugrel, Ticagrelor or Ticlopidine for a minimum of one (1) month post procedure.
- It is very important that the patient comply with the post-procedural antiplatelet therapy recommendations. Early discontinuation of prescribed antiplatelet medication could result in a higher risk of thrombosis, MI, or death. Prior to percutaneous coronary intervention (PCI), if the patient is required to undergo a surgical or dental procedure that might require early discontinuation of antiplatelet therapy, the physician and patient should carefully consider whether a COBRA PzF NanoCoated Coronary Stent System and its associated recommended antiplatelet therapy is the appropriate PCI treatment of choice. Following PCI, should a surgical or dental procedure be necessary, requiring suspension of antiplatelet therapy, the risks and benefits of the procedure should be weighed against the possible risk associated with early discontinuation of antiplatelet therapy. Patients who require early discontinuation of antiplatelet therapy should be monitored carefully for cardiac events. At the discretion of the patient's treating physicians, the antiplatelet therapy should be restarted as soon as possible.

6.3 Precautions: Use in Conjunction with Other Procedures

The safety and effectiveness of using mechanical atherectomy devices or laser angioplasty catheters in conjunction with the COBRA PzF NanoCoated Coronary Stent System implantation have not been established.

6.4 Precautions: Lesion / Vessel Characteristics

Safety and effectiveness of the COBRA PzF NanoCoated Coronary Stent System have not been established for subject populations with the following clinical settings:

- Unresolved vessel thrombus at the lesion site
- Coronary artery reference vessel diameters < 2.50 mm or > 4.00 mm
- Lesion lengths > 24 mm or lesions requiring more than one COBRA PzF NanoCoated Coronary Stent
- Lesions located in saphenous vein grafts
- Lesions located in unprotected left main coronary artery, ostial lesions, and lesions located at bifurcations
- Previously stented lesions
- Diffuse disease or poor flow (TIMI < 1) distal to the identified lesions
- Excessive tortuosity proximal to or within the lesion
- Recent acute myocardial infarction (AMI) or evidence of thrombus in the target vessel
- Multivessel disease
- In-stent restenosis
- Patients with a chronic total occlusion

6.5 Precautions: Magnetic Resonance Imaging (MRI)

The COBRA PzF NanoCoated Stent is MR Conditional.

MR Conditional

Non-clinical testing demonstrated that the COBRA PzF NanoCoated Stent is MR Conditional for single and overlapping stents up to 58mm. A patient with this device can be scanned safely, immediately after placement under the following conditions:

- Static magnetic field of 1.5-Tesla and 3.0-Tesla, only
- Maximum spatial gradient magnetic field of 4,500-Gauss/cm (45 T/m) or less
- Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 4-W/kg (First Level Controlled Mode)

MRI Related Heating

Non-clinical testing, demonstrated that the COBRA PzF NanoCoated Stent is MR Conditional for single and overlapping stents and produced the following temperature rises during MRI performed for 15-min of scanning (i.e., per pulse sequence) in 1.5-Tesla/64-MHz (Magnetom, Siemens Medical Solutions, Malvern, PA. Software Numaris/4, Version Syngo MR 2002B DHHS Active-shielded, horizontal field scanner) and 3-Tesla/128-MHz(Excite, HDx, Software 14X.M5, General Electric Healthcare, Milwaukee, WI) MR systems:

	1.5-Tesla	3-Tesla
MR system reported, whole body averaged SAR	2.9-W/kg	2.9-W/kg
Calorimetry measured values, whole body averaged SAR	2.1-W/kg	2.7-W/kg
Highest temperature change	2.6 °C	3.0 °C
Temperature scaled to whole body averaged SAR of 4-W/kg	3.6 °C	4.1 °C

The effect of heating in the MRI environment for stents with fractures is not known.

Artifact Information

MR image quality may be compromised if the area of interest is in the exact same area or relatively close to the position of the COBRA PzF NanoCoated Stent. Therefore, optimization of MR imaging parameters to compensate for the presence of this device may be necessary. The maximum artifact size (i.e., as seen on the gradient echo pulse sequence) extends approximately 5-mm relative to the size and shape of this implant. The lumen of this stent cannot be visualized using these pulse sequences.

6.6 Precautions: Stent Handling

- Each stent is for single use only. Do not resterilize or reuse this device. Note the "Use By" (expiration) date on the product label.
- The delivery system should not be used in conjunction with other stents.
- Use caution to not disrupt the pre-mounted stent during removal of the delivery balloon from the packaging, placement over the guidewire, or advancement through hemostasis valve into the guide catheter.
- Do not touch, handle, manipulate ("roll" or twist), or remove the pre-mounted stent as this may cause contamination, stent damage and/or dislodgement from the delivery balloon. These components are intended to perform together as a system.
- Do not suspend the pre-mounted stent within a solution on the sterile field.
- Use only the appropriate inflation medium (i.e., 1:1 solution by volume of contrast medium and saline). Never use air or other gaseous medium to inflate the balloon.

6.7 Precautions: Stent Placement

6.7.1 Precautions: Stent Preparation

- Do not pre-inflate the delivery system prior to stent deployment.
- When introducing the stent delivery system into a vessel, do not induce negative pressure on the delivery system as this may cause stent dislodgement from the balloon.
- Use guiding catheters which have lumen sizes that are suitable to accommodate the stent delivery system (see section 1.1 Device Component Description).
- An unexpanded stent should be introduced into the coronary arteries one time only. An unexpanded stent should not be reintroduced into the artery once it has been pulled back into the guiding catheter. Subsequent movement in and out through the distal end of the guiding catheter should not be performed, as the stent may be damaged or dislodged during retraction back into the guiding catheter.

6.7.2 Precautions: Stent Implantation

- The decision to pre-dilate the lesion with an appropriate size balloon should be carefully based on patient and lesion characteristics.
- The COBRA PzF NanoCoated stent should be positioned using standard angiographic techniques under direct visualization using high-resolution fluoroscopy.

- Do not expand the stent if it is not properly positioned in the vessel. Once deployment begins, the stent cannot be repositioned.
- Do not attempt to pull an unexpanded stent retrogradely through guiding catheter (See Section 6.8 for Precautions: Stent System Removal).
- The delivery system should not be rotated during the deployment procedure. Do not rotate the delivery system by more than one rotation in either direction during use.
- Stent implantation may lead to vessel dissection and may cause abrupt closure necessitating further intervention (e.g., CABG, additional dilatation and/or stent placement, or other).
- Balloon pressures should be monitored during inflation. Do not exceed the rated burst pressure (RBP) as indicated on the product label. Use of pressures higher than product label specifications may result in a ruptured balloon causing possible intimal damage and dissection.
- Stent implantation has the potential to compromise side branch patency.

6.8 Precautions: Stent System Removal

- An unexpanded stent should not be reintroduced into the artery once it has been pulled back into the guiding catheter. Subsequent movement in and out through the distal end of the guiding catheter should not be performed, as the stent may be damaged or dislodged during retraction back into the guiding catheter.
- Remove the entire system as a single unit if:
    - Unable to cross the lesion easily.
    - Resistance is encountered anytime during either stent advancement across the lesion or removal of the delivery catheter after deployment.

- If removal of an unexpanded stent from the patient is required, do not pull the underdeployed stent retrogradely into the guide catheter. Perform the following:
    1. Advance the coronary guidewire as far distally into the coronary vasculature as safely possible. The stent/balloon catheter should be withdrawn until the proximal end of the stent is aligned with the distal end of the guide catheter.
    2. Tighten the hemostatic valve to secure the delivery system to the guide catheter.
    3. The guide catheter, stent/balloon catheter system, and guidewire should then be removed as one unit through the introducer sheath.

  Failure to follow these steps and/or applying excessive force on the delivery system may result in damage to, or loss of, the stent and/or delivery system components.

- Stent retrieval methods (e.g., use of additional wires, snares and/or forceps) may result in additional trauma to the coronary vasculature and/or the vascular access site. Complications may include bleeding, hematoma, pseudoaneurysm, or perforation.
- If the balloon ruptures during stent expansion, withdraw the balloon and exchange for a new balloon catheter to complete stent deployment.

6.9 Precautions: Post Deployment

- Use caution when crossing a newly deployed stent with a coronary guidewire, balloon, delivery system, or intravascular ultrasound to avoid disruption of stent geometry and stent migration/dislodgement.
- If patient requires imaging, see Section 6.5 Precautions: Magnetic Resonance Imaging (MRI).

7.0 OVERVIEW OF CLINICAL EXPERIENCE

The safety and effectiveness of the COBRA PzF NanoCoated Coronary Stent System have been demonstrated in the PzF SHIELD trial. The PzF SHIELD trial is a global trial which enrolled 296 patients with symptomatic ischemic heart disease in the United States, Germany, France, Latvia, Serbia, Spain and Switzerland.

8.0 ADVERSE EVENTS

8.1 Observed Adverse Events

Adverse events experience presented in this section were observed in the PzF SHIELD trial and have been adjudicated by the Clinical Events Committee. Major clinical events of the PzF SHIELD study are presented in table 8.1-1.

Table 8.1-1 PzF SHIELD Major Clinical Events from post procedure to 270 day follow up

Event	PzF SHIELD Trial (N = 296)		
Safety Measures	**To 30 days [1]**	**To 180 days [2]**	**To 270 days [3]**
All death	0.34% (1/296)	1.70% (5/294)	2.06% (6/291)
Cardiac death	0.34% (1/296)	0.34% (1/292)	0.35% (1/286)
MI (historical definition)	5.76% (17/295)	5.84% (17/291)	5.96% (17/285)
Q-wave MI	0.00% (0/295)	0.00% (0/291)	0.00% (0/285)
Non Q-wave MI	5.76% (17/295) [4]	5.84% (17/291)	5.96% (17/285)
MI (ARC definition)	6.10% (18/295)	6.87% (20/291)	7.02 % (20/285)
TLR	0.00% (0/295)	2.41% (7/291)	5.61% (16/285)
Clinically driven TLR	0.00% (0/295)	2.41% (7/291)	4.56% (13/285)
TVR	0.68% (2/295)	3.44% (10/291)	7.34% (21/286)
Clinically driven TVR	0.34% (1/295)	3.09% (9/291)	5.94% (17/286)
Cardiac death or MI (historical definition)	6.08% (18/296)	6.16% (18/292)	6.29% (18/286)
Cardiac death or MI (ARC definition)	6.42% (19/296)	7.19% (21/292)	7.34% (21/286)
MACE (historical definition)	6.08% (18/296)	7.88% (23/292)	10.14% (29/286)
TVF	6.42% (19/296)	8.56% (25/292)	11.50% (33/287)
Ischemic or hemorrhagic stroke	0.00% (0/295)	0.34% (1/292)	0.35% (1/286)
Early stent thrombosis [ARC definition] (≤ 30 days)	0.00% (0/295)	N/A	N/A
Late stent thrombosis [ARC definition] (> 30 days)	N/A	0.00% (0/291)	0.00% (0/285)

[1] Events defined for the period of 30 days post-procedure follow-up are reported for patients with at least 23 days of follow-up or with event to 30 days.

[2] Events defined for the period of 180 days post-procedure follow-up are reported for patients with at least 150 days of follow-up or with event to 180 days.

[3] Events defined for the period of 270 days post-procedure follow-up are reported for patients with at least 240 days of follow-up or with event to 270 days.

[4] 17/296 were periprocedural NQWMI (Historical definition- CKMB > 3x UNL).

8.2 Potential Adverse Events

Potential adverse events associated with stent placement include, but are not limited to:

- Abrupt closure
- Access site pain, hematoma, or hemorrhage
- Allergic/reactions (including to contrast media, stent materials or medication)
- Angina
- Aneurysm (Coronary)
- Arteriovenous fistula
- Arrhythmias, including ventricular tachycardia or fibrillation
- Bleeding
- Cardiac tamponade
- Cardiogenic shock
- Cardiomyopathy
- Death
- Emboli (including air, tissue, plaque, thrombus or device materials)
- Failure to deliver stent to intended site
- Heart failure
- Hematoma

- Hypotension and/or hypertension
- Infection, local and/ or systemic
- Ischemia, myocardial
- Myocardial infarction
- Pericardial effusion
- Pseudoaneurysm
- Pulmonary edema
- Renal insufficiency or failure
- Respiratory failure
- Restenosis of the stented segment
- Shock
- Stent fracture or deformation
- Stent migration
- Stent thrombosis
- Stroke or transient ischemic attack (TIA)
- Total vessel occlusion
- Vessel spasm
- Vessel injury (including dissection, perforation, rupture or trauma)

9.0 CLINICAL STUDIES

PzF SHIELD Trial

9.1 Primary Objective

To assess the safety and effectiveness of the COBRA PzF NanoCoated Coronary Stent System for the treatment of subjects with symptomatic ischemic heart disease due to a single de novo lesion contained within a native coronary artery with reference vessel diameter between 2.5 mm and 4.0 mm and lesion length ≤24 mm by visual estimation.

9.2 Design

The PzF SHIELD is a prospective, single arm, multicenter trial conducted in the United States and Europe. Patients were eligible for enrollment if: they were ≥ 18 years of age with stable angina or unstable angina pectoris or a positive functional ischemia study and a left ventricular ejection fraction (LVEF) ≥ 30%; and have a single de novo lesion within a native coronary artery with reference vessel diameter between 2.5 mm and 4.0 mm and lesion length ≤ 24 mm and stenosis of ≥ 70% and < 100% by visual estimate with TIMI flow >1. The protocol recommended aspirin indefinitely and recommended Clopidogrel, Prasugrel, Ticagrelor or Ticlopidine for a minimum of one (1) month post procedure.

Baseline and post-procedure angiographic data were evaluated by QCA at a designated angiographic core laboratory. ECGs were also reviewed and evaluated at a designated central laboratory. Major clinical events, including stent thrombosis, were adjudicated by an independent Clinical Event Committee.

The primary endpoint was the incidence of target vessel failure (TVF): cardiac death, target vessel myocardial infarction (MI) [Q wave or non-Q wave, ARC-definition], or clinically driven target vessel revascularization (TVR) by percutaneous or surgical methods within 270 days post-procedure. This rate was compared with a predefined performance goal (PG) of 19.6%, which was derived using a meta-analysis of literature reporting outcomes with bare metal coronary stents. In-stent late loss (LL) at 270 day post-procedure was a powered secondary endpoint for this trial. The LL was compared to a predefined PG of 1.1 mm.

A total of 296 patients were enrolled at a total of 35 clinical sites in the U.S. and Europe. Of the 296 total patients enrolled in the ITT population, 287 were evaluable as part of the primary and secondary clinical endpoint analyses for this 270 day analysis period.

Patients were followed at 30, 180, 270, and 360 days. Additional annual follow up is ongoing for up to five (5) years.

Demographics:

Patients had an overall mean age of 66.5 years. 70.3% were men. 14.9% had prior MI. 30.4% had prior percutaneous coronary intervention. 33.7% had diabetes mellitus requiring medications. 12.24% had atrial fibrillation. 82.7% had hypertension, and 80.6% had hyperlipidemia.

Baseline lesion characteristics:

The mean RVD was 2.74 ± 0.48 mm, and the mean minimal luminal diameter (MLD) was 0.9 ± 0.36 mm. The mean percent stenosis was 63.95% ± 11.43 pre-procedure and the mean lesion length was 12.77 ± 6.45 mm. 52.51% of lesions were type B2 and 19.4% were type C.

Procedure characteristics:

Procedure Details	ITT Population (N=296 Patients, N=300 Lesions)
Total procedure time (minutes)	
Mean ± SD (N)	30.70 ± 15.68 (296)
Median	27.50
Range (Min, Max)	(5.00, 95.00)
Total Fluoroscopy time (minutes)	
Mean ± SD (N)	10.80 ± 6.18 (296)
Median	9.75
Range (Min, Max)	(0.20, 42.00)
Pre-Dilatation Details	
Pre-dilatation performed	96.28% (285/296)
Balloons used	100.00% (285/285)
One (1) balloon used	96.49% (275/285)
Two (2) balloons used	2.81% (8/285)
Three (3) or more balloons used	0.70% (2/285)
Total Pre-Dilatation Time (minutes)	
Mean ± SD (N)	12.73 ± 2.70 (285)
Median	12.45
Range (Min, Max)	(7.28, 20.50)
Dissection Details	
Dissection occurred [PER]	5.76% (17/295)
Grade A	64.71% (11/17)
Grade B	17.65% (3/17)
Grade C	17.65% (3/17)
Grade D	0.00% (0/17)
Grade E	0.00% (0/17)
Grade F	0.00% (0/17)
Post-Dilatation Details	
Post-dilatation performed	48.31% (143/296)
Procedural Medications	
Aspirin (Pre-Procedure)	94.93% (281/296)
P2Y12 Blocker	98.65% (292/296)
Clopidogrel	84.46% (250/296)
Ticagrelor	7.43% (22/296)
Prasugrel	6.42% (19/296)
Others	0.34% (1/296)
Anticoagulant	99.32% (294/296)
Heparin	72.30% (214/296)
Bivalirudin	27.03% (80/296)
Glycoprotein IIb/IIIa inhibitors	6.08% (18/296)
Activated Clotting Time [ACT] Monitoring for Heparin (seconds)	
Mean ± SD (N)	320.51 ± 98.25 (201)
Median	300.00
Range (Min, Max)	(93.00, 825.00)

9.3 Primary Endpoint Results (270 days TVF)

The primary endpoint at 270 days post procedure was met. The 270 days TVF rate was 11.50%. The upper bound one-sided 95% CI of 15.07% was below the predefined PG of 19.62%.

Population	COBRA PzF NanoCoated Coronary Stent System	95% CI	Upper Bound of 95% one-sided CI	Performance Goal
ITT (N = 296)	11.50% (33/287)	[8.05%, 15.77%]	15.07%	19.62%

9.4 Secondary Endpoint Results (270 days)

Endpoints	PzF SHIELD (N = 296)
All cause mortality	2.06% (6/291)
Cardiac mortality	0.35% (1/286)
MI (historical definition)	5.96% (17/285)
Q-wave MI	0.00% (0/285)
Non Q-wave MI	5.96% (17/285) [1]
MI (ARC definition)	7.02% (20/285)
TLR	5.61% (16/285)
Clinically driven TLR	4.56% (13/285)
TVR	7.34% (21/286)
Clinically driven TVR	5.94% (17/286)
Composite endpoint of cardiac death and MI (historical definition)	6.29% (18/286)
Composite endpoint of cardiac death and MI (ARC definition)	7.34% (21/286)
MACE (historical definition)	10.14% (29/286)
TVF	11.50% (33/287)
Ischemic or hemorrhagic stroke	0.35% (1/286)
Late stent thrombosis (> 30 days)	0.00% (0/285)
Early Stent Thrombosis [ARC definition] (≤ 30days)	0.00% (0/295)
Acute Success Rates	
Device Success [2]	100.00% (291/291)
Lesion Success [3]	100.00% (292/292)
In stent late lumen loss (LL) [4]	
Mean ± SD (N)	0.84 ± 0.48 (113)

[1] 17/296 were periprocedural NQWMI (Historic definition- CKMB > 3x UNL).

[2] Defined as the attainment of <30% final residual stenosis of the target lesion using only the COBRA PzF NanoCoated Coronary Stent System.

[3] Defined as the attainment of <30% final residual stenosis of the target lesion using any percutaneous method.

[4] Powered secondary endpoint.

9.5 Sub-group Analysis

Pre-specified subgroup analyses for the study endpoints were performed based on: gender; angiographic cohort versus clinical (non-angiographic) cohort; U.S. versus non-U.S. populations; and diabetic patients versus non-diabetic patients. Analyses of primary and secondary endpoints by gender and angiographic cohort versus clinical cohorts resulted in no endpoint measures where a statistically significant difference was observed.

9.5.1 Gender

The PzF SHIELD study was not powered to study safety or effectiveness of the COBRA PzF NanoCoated stent in gender-specific subgroups. However, a pre-specified analysis of primary and secondary endpoints by gender was performed. Analysis showed similar treatment effect between genders. This suggests that the overall conclusion of the trial regarding both safety and effectiveness can be generalized to males and females.

Endpoints	Males (N = 208)	Females (N = 88)	p-value
Primary Endpoints (270 days)			
TVF [1]	11.4% (23/202)	11.8% (10/85)	1.000
Cardiac death	0.5% (1/202)	0.0% (0/85)	1.000
Target vessel myocardial infarction (MI)	5.4% (11/202)	7.1% (6/85)	0.591
Clinically TVR	5.4% (11/202)	7.1% (6/85)	0.591
Secondary Endpoints (270 days)			
All Causes Mortality	2.0% (4/204)	2.3% (2/87)	1.000
Cardiac Mortality	0.5% (1/201)	0.0% (0/85)	1.000
MI (historical definition)	5.5% (11/200)	7.1% (6/85)	0.594
Q-wave MI	0.0% (0/200)	0.0% (0/85)	--
Non Q-wave MI	5.5% (11/200)	7.1% (6/85)	0.594
MI (ARC definition)	6.5% (13/200)	8.2% (7/85)	0.616
TLR	5.5% (11/200)	5.9% (5/85)	1.000
Clinically driven TLR	4.5% (9/200)	4.7% (4/85)	1.000
TVR	6.5% (13/201)	9.4% (8/85)	0.457
Clinically driven TVR	5.5% (11/201)	7.1% (6/85)	0.593
Composite endpoint of cardiac death and MI (historical definition)	6.0% (12/201)	7.1% (6/85)	0.791
Composite endpoint of cardiac death and MI (ARC definition)	7.0% (14/201)	8.2% (7/85)	0.804
MACE (historical definition)	10.4% (21/201)	9.4% (8/85)	1.000
Ischemic or hemorrhagic stroke	0.5% (1/201)	0.0% (0/85)	1.000
Early Stent Thrombosis [ARC definition] (≤ 30days)	0.0% (0/207)	0.0% (0/88)	--
Late Stent Thrombosis (> 30 days)	0.0% (0/200)	0.0% (0/85)	--
Acute Success Rates			
Device Success [2]	100.0% (205/205)	100.0% (87/87)	--
Lesion Success [3]	100.0% (205/205)	100% (87/87)	--

[1] Events defined for the period of 270 days post-procedure follow up are reported for patients with at least 240 days of follow-up or with a composite primary endpoint to 270 days.

[2] Defined as the attainment of < 30% final residual stenosis of the target lesion using only the COBRA PzF NanoCoated Coronary Stent System.

[3] Defined as the attainment of < 30% final residual stenosis of the target lesion using any percutaneous method.

9.5.2 Diabetes

Endpoints	Patients with Diabetes (N = 99)	Patients without Diabetes (N = 195)	p-value
Primary Endpoints (270 days)			
TVF [1]	6.3% (6/96)	13.8% (26/189)	0.073
Cardiac death	1.0% (1/96)	0.0% (0/189)	0.337
Target vessel MI	2.1% (2/96)	7.4% (14/189)	0.099
Clinically driven TVR	4.2% (4/96)	6.9% (13/189)	0.437
Secondary Endpoints (270 days)			
All cause mortality	3.1% (3/98)	1.6% (3/191)	0.411
Cardiac mortality	1.0% (1/96)	0.0% (0/188)	0.338
MI (historical definition)	2.1% (2/95)	7.4% (14/188)	0.099
Q-wave MI	0.0% (0/95)	0.0% (0/188)	--
Non Q-wave MI	2.1% (2/95)	7.4% (14/188)	0.099
MI (ARC definition)	2.1% (2/95)	9.0% (17/188)	0.041
TLR	4.2% (4/95)	6.4% (12/188)	0.590
Clinically driven TLR	3.2% (3/95)	5.3% (10/188)	0.554
TVR	5.3% (5/95)	8.5% (16/189)	0.472
Clinically driven TVR	4.2% (4/95)	6.9% (13/189)	0.438
Composite endpoint of cardiac death and MI (historical definition)	3.1% (3/96)	7.4% (14/188)	0.190
Composite endpoint of cardiac death and MI (ARC definition)	3.1% (3/96)	9.0% (17/188)	0.085
MACE (historical definition)	5.2% (5/96)	12.2% (23/188)	0.090
Ischemic or hemorrhagic stroke	0.0% (0/95)	0.5% (1/189)	1.000
Early Stent Thrombosis [ARC definition] (≤ 30days)	0.0% (0/98)	0.0% (0/195)	--
Late stent thrombosis (> 30 days)	0.0% (0/95)	0.0% (0/188)	--
Acute Success Rates			
Device Success [2]	100.0% (98/98)	100.0% (192/192)	--
Lesion Success [3]	100% (98/98)	100% (192/192)	--

[1] Events defined for the period of 270 days post-procedure follow up are reported for patients with at least 240 days of follow-up or with a composite primary endpoint to 270 days.

[2] Defined as the attainment of < 30% final residual stenosis of the target lesion using only the COBRA PzF NanoCoated Coronary Stent System.

[3] Defined as the attainment of < 30% final residual stenosis of the target lesion using any percutaneous method.

9.6 Conclusions

The 270-day results of the PzF SHIELD trial show the COBRA PzF stent and delivery system to be safe and effective in the treatment of symptomatic ischemic heart disease due to a single de novo lesion contained within a native coronary artery when compared to the performance goal.

10.0 PATIENT SELECTION AND TREATMENT

Individualization of treatment

The risks and benefits should be considered for each patient before using COBRA PzF stent. Patient selection factors to be assessed should include a medical judgment regarding the risk of long-term antiplatelet therapy. Antiplatelet drugs should be used in combination with COBRA PzF stents. Physicians should consider the patient's individual needs to determine the specific antiplatelet / anticoagulation regimen to be used for their patients in general practice. In the PzF SHIELD trial, the protocol recommended aspirin indefinitely and recommended Clopidogrel, Prasugrel, Ticagrelor or Ticlopidine for a minimum of one (1) month post procedure.

Premorbid conditions that increase the risk of poor initial results or the risk of emergency referral for bypass surgery (diabetes mellitus, heart failure, renal failure, high risk for bleeding and severe obesity) should be reviewed.

11.0 PATIENT COUNSELING AND INFORMATION

Physicians should consider the following in counselling patients about this product:

- Discuss the risks associated with stent placement
- Discuss the risks of early discontinuation of the antiplatelet therapy
- Discuss the risk / benefit issues for this particular patient
- Discuss alternation to current life style immediately following the procedure and over the long term

The following patient materials are provided for this product:

- A Patient Information Guide including information on coronary artery disease, coronary artery stenting and the COBRA PzF NanoCoated Coronary Stent System
- Stent Implant Card, including both patient information and stent implant information

12.0 OPERATOR'S INSTRUCTIONS

12.1 Materials Required but Not Included

- Appropriate guiding catheter(s)
- 1 - 2 syringes (20 ml)
- 1,000 u / 500 ml heparinized normal saline
- 0.014" (0.36 mm) x 175 cm (minimum length) guide wire
- Rotating hemostatic valve
- Contrast diluted 1:1 with heparinized normal saline
- Inflation device
- Pre-deployment dilatation catheter
- Three-way stopcock
- Torque device
- Guide wire introducer
- Appropriate arterial sheath
- Appropriate anticoagulation and antiplatelet drugs

12.2 Prior to Use

1. Select the stent size appropriate for the intended use.
2. Carefully inspect the product label and verify that the product size is appropriate for the intended use.
3. Carefully inspect the sterile package before opening. It is not recommended that the product be used after the "Use By" date. If the integrity of the sterile package has been compromised prior to the product "Use By" date (e.g., damage of the package) contact CeloNova BioSciences at 1-888-388-3888 for return information.
4. If the sterile package appears intact, open sterile packaging and transfer contents into sterile field.
5. Carefully remove the system from the package and inspect for bends, kinks and other damage.
6. Remove protective cover and stylet by gently grasping the distal end of the cover and withdrawing distally. Verify that the stent is located between the radiopaque markers.

   NOTE: Do not use if any defects are noted.

12.3 Delivery System Preparation

1. Flush the guidewire lumen with sterile heparinized normal saline solution.

   NOTE: Hydrophilic coating has been applied to the delivery system, between the guide wire notch and the proximal balloon bond.

2. Prepare a 20 cc capacity inflation device/syringe with diluted contrast media (1:1 by volume contrast media and sterile saline).

3. Attach the inflation device/syringe to the inflation port of the stent system using a 3-way stopcock.
4. Apply negative pressure to create a vacuum to remove any residual air from the delivery catheter and balloon. Repeat as needed.

   NOTE: Do not use the stent delivery system if it will not hold negative pressure. Failure to maintain vacuum is an indication of system failure.

12.4 Delivery Procedure

1. Prepare the patient for a PTCA procedure according to the institution's standard clinical practice.
2. Pre-dilate the lesion according to the institution's standard clinical practice.
3. Release any negative pressure previously applied to the stent delivery system via the inflation device. Ensure that the stent delivery system is at neutral pressure before proceeding.
4. Open the hemostatic valve.
5. While maintaining guidewire position across the lesion, back load the guidewire into the distal tip of the stent system.
6. Advance the stent delivery system into the guide catheter and tighten hemostatic valve.

   NOTE: Should any resistance be felt at any time during stent system advancement, the entire system should be removed as a single unit. See Section 6.8 for Precautions: Stent System Removal.

12.5 Deployment Procedure

1. While maintaining stable guide catheter seating and placement across the target lesion, advance the stent across the target lesion.
2. Verify the stent placement using the proximal and distal balloon markers and high-resolution fluoroscopy to ensure adequate stent coverage at both the proximal and distal margins of the lesion.

   NOTE: If any stent movement occurs during the positioning of the stent delivery system, do not deploy the stent. The entire system should be removed as a single unit. See Section 6.8 for Precautions: Stent System Removal.
3. Deploy the stent by inflating the stent system balloon to at least nominal pressure (NOM) — but not beyond Rated Burst Pressure (RBP) — in accordance with compliance chart (see Table 12.5-1). Hold the pressure for 15 30 seconds to expand the stent so that it is in complete apposition with the arterial wall. If necessary, the stent system may be re-inflated or further inflated, up to rated burst pressure, to assure complete apposition of the stent to the artery wall.

   NOTE: Do not exceed Rated Burst Pressure (RBP) — see Table 12.5-1

   NOTE: If the stent is not completely apposed to the vessel wall, under-expansion may result in stent movement. The stent should be re-crossed and further expanded with another appropriate sized balloon. Use caution during subsequent dilatations to limit barotrauma outside the stent margins.

	Pressure (ATM)	Stent Inner Diameter (mm)				
		2.50	**2.75**	**3.00**	**3.50**	**4.00**
NOM	**10**	2.45	2.71	2.91	3.48	3.90
	11	2.50	2.75	2.96	3.53	3.96
	12	2.55	2.80	3.01	3.58	4.01
	13	2.59	2.85	3.07	3.63	4.06
	14	2.64	2.91	3.12	3.67	4.10
	15	2.69	2.95	3.16	3.73	4.15
RBP	**16**	2.74	3.00	3.21	3.78	4.20
	17	2.78	3.05	3.26	3.83	
	18	2.83	3.10	3.31	3.87	

Table 12.5-1 – COBRA PzF NanoCoated Coronary Stent System Compliance Chart

12.6 Post Deployment Removal Procedure

1. Deflate the balloon completely by pulling negative pressure on the inflation device for at least 15 seconds. Larger balloons may take longer to fully deflate. Confirm full deflation under fluoroscopy.
2. With the hemostatic valve fully open and while maintaining vacuum on the inflation device, slowly withdraw the balloon from the stent.
3. With stable guidewire and guide catheter positioning, slowly withdraw the deliverysystem while maintaining negative pressure on the inflation device.
4. Tighten the hemostatic valve.

   NOTE: Should any resistance be felt at any time during removal of the delivery system post stent implantation, the entire system should be removed as a single unit. See Section 6.8 for Precautions: Stent System Removal

12.7 Post Procedure Assessment

- Repeat angiography to assess the stented area, ensuring that the stent has been adequately expanded. If the final stent diameter does not match the reference vessel diameter, perform post dilatation with an appropriate sized balloon.

  Post Deployment Dilatation of Stented Segments

  Precaution: Do not dilate the stent beyond the limits tabulated below:

Nominal Stent Inner Diameter (ID)	Maximum Dilatation ID*
2.50, 2.75 and 3.00	3.40mm
3.50	4.25mm
4.00	4.50mm

  *maximum stent inner diameter

- All efforts should be taken to assure the stent is not under-expanded. If the deployed stent size is still inadequate with respect to vessel diameter, or if full contact or apposition with the vessel wall is not achieved, a post dilatation with a larger diameter balloon may be used to optimize the stent expansion. The stent may be expanded using a low profile and high pressure balloon catheter. If this is required, the stented segment should be re-crossed carefully with a prolapsed guidewire to avoid migration or movement of the stent. The balloon should be centered within the stent and should not extend outside of the stented region.

13.0 DISCLAIMER OF WARRANTY AND LIMITATIONS

Descriptions or specifications in this document are intended to provide physicians with information relating to the COBRA PzF NanoCoated Coronary Stent System product description, safe handling procedures, and potential risks inherent to the procedure, and do not constitute a guarantee. There is no express or implied warranty, including without limitation, any implied warranty of merchantability or fitness for a particular purpose. Under no circumstances shall CeloNova BioSciences, Inc. be liable for any direct, incidental, or consequential damages. No person has the authority to bind CeloNova BioSciences, Inc. to any representation or warranty except as specifically set forth herein.

Descriptions or specifications in CeloNova BioSciences, Inc. printed materials, including this publication, are meant solely to generally describe the product at the time of manufacture and do not constitute any express warranties.

14.0 PATENTS AND TRADEMARKS

This product and/or its use is covered by U.S. and foreign pending and issued patents. COBRA PzF, design, PzF and Polyzene are trademarks of CeloNova BioSciences, Inc.

15.0 EXPLANATION OF SYMBOLS USED ON THE PACKAGE LABEL

	Do Not Resterilize
	Do Not Use if Package is Damaged
LOT	Lot Number
REF	Catalog Number
	Consult Instructions for Use
STERILE EO	Sterilized using Ethylene Oxide
	MR Conditional
	Do Not Reuse
	Package Quantity
	Use By
	Manufacturer

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COBRA PzF NCS

NanoCoated Coronary Stent System

Stent System Compliance Chart

	Pressure (ATM)	Stent Inner Diameter (mm)				
		2.50	**2.75**	**3.00**	**3.50**	**4.00**
NOM	**10**	2.45	2.71	2.91	3.48	3.90
	11	2.50	2.75	2.96	3.53	3.96
	12	2.55	2.80	3.01	3.58	4.01
	13	2.59	2.85	3.07	3.63	4.06
	14	2.64	2.91	3.12	3.67	4.10
	15	2.69	2.95	3.16	3.73	4.15
RBP	**16**	2.74	3.00	3.21	3.78	4.20
	17	2.78	3.05	3.26	3.83	
	18	2.83	3.10	3.31	3.87	

Manufacturer:
CeloNova BioSciences, Inc.
5840 El Camino Real, Suite 111
Carlsbad, CA 92008 USA
+1 888.388.3888

CELO NOVA BIOSCIENCES