NeoCor

INSTRUCTIONS FOR USE

UniLine Aortic Biological Preserved Heart Valve Prosthesis
with Technical Specification (TU) 9444-010-57628698-2008
(hereinafter, the valve)

Sterile components: UniLine valve and holder (handle and holder).
Non-sterile components: exterior of the storage container.

Symbol	Designation	Symbol	Designation
	Consult the Instructions for Use		Do Not Reuse
	Sterilized using aseptic technique		Do Not Use if Package is Damaged
	Catalog Number		Use By
	Caution! Consult the Instructions for Use		Temperature Range
	Manufacturer		Serial Number
	Sterilized Using Liquid Chemical Sterilant		Do Not Resterilize
	Treated with sodium hydroxide		

VALVE DESCRIPTION:

UniLine aortic valve (see Figure 1) is a stented valve with xenopericardium leaflets, designed for supra-annular implantation in the aortic position. The valve design features a stent assembly consisting of the polypropylene form and nitinol wire covered with pericardium. The valve stent cover made of the biological tissue allows to perform special treatment of its entire surface.
The valve cuff only partially shapes the contour matching that of the native annulus.
Valve leaflets are made of bovine pericardium. Ethylene glycol diglycidyl ether is used to chemically cross-link the pericardium. Anti-prion treatment of the pericardium is performed with 1 molar sodium hydroxide for 60–75 minutes at 20–25°C.The UniLine valves are sterilized with a liquid chemical agent: 1% chlorhexidine. The UniLine valve is supplied sterile. The valve manufacturing process includes anticalcification treatment. The valve is stored in a 0.3% paraben mix solution.

Valve Design Variants

Size, mm	Catalog number REF
21	ULA21s
23	ULA23s
25	ULA25s
Type of treatment:	
Anticalcification	

The scope of delivery includes:

Component	Quantity, pcs.
UniLine valve	1
Holder (handle and holder)	1
Container filled with the storage solution	1
Instructions for Use	1
Implantation registration form	1
Identification stickers	2
Carton	1
Carton insert	2

INDICATIONS
UniLine valve is intended for use in cardiac surgery as a substitute of the incompetent native aortic valve or a previously implanted heart valve prosthesis.

CONTRAINDICATIONS
None known. They are determined by a physician in each individual case.

WARNINGS
- For single use only.
- Do not resterilize the valve by any method.
- The valve size depends on the size of the recipient annulus and anatomical features of the sinotubular junction. Implantation of the valve with a size larger than that of the annulus is not recommended, as it may result in stent deformation, valvular incompetence, and/or damage to the surrounding tissues. Do not use an inappropriately large valve! The valve dimensions are presented in Table 1. Perform preoperative echocardiography to select an optimal valve size.
- Passage of a catheter through any part of the bioprosthesis may damage the valve and is therefore not recommended.
- Accelerated deterioration due to calcific degeneration of the UniLine valve may occur in:
  - Children, adolescents, or young adults
  - Patients with altered calcium metabolism (e.g., patients with hyperparathyroidism or chronic renal failure)
  - Individuals requiring hemodialysis
- Maintenance and repair of the valve are not provided for by the manufacturer and are not required for its intended use. The valve prostheses are intended for single use only and must not be resterilized.

Do not use the device if:
- The expiration date indicated on the carton has elapsed.
- If the temperature indicator has changed its color, or if the valve has been improperly stored in temperature conditions outside of the +5°C to +40°C
- The tamper-evident film is damaged, broken, or missing, or if fluid is leaking from the container.

range.
- The storage solution does not completely cover the valve.
- The valve sterility has been compromised; the valve has been damaged, or if there are any other defects.

PRECAUTIONS

- The safety and efficacy of the UniLine valve have not been studied in the following specific populations:
  - Pregnant women
  - Nursing mothers
  - Patients with chronic kidney failure
  - Patients with aneurysmal aortic degenerative conditions
  - Patients with active endocarditis
  - Children, adolescents, or young adults
- The holder handle is supplied sterile. Make sure that the "sterile until" date indicated on the carton has not elapsed. Do not use the holder handle if there are cracks or any other signs of deformation on it.
- Position the valve so that the stent does not obstruct the coronary ostia.
- Do not place the non-sterile valve storage container in the sterile field.
- Do not expose the valve to solutions other than the storage solution in which it is supplied by the manufacturer.
- The sterile saline is used to rinse the valve and irrigate it during implantation.
- Do not add antibiotics to either the valve storage solution or the rinse solution.
- Do not apply antibiotics to the valve.
- Do not allow the valve tissue to dry. Place the valve in the sterile saline rinse solution immediately upon removal from the valve storage solution. The valve must be periodically irrigated during implantation.
- Do not implant the valve without thoroughly rinsing as directed.
- Use caution during suturing though the cuff to avoid laceration of the valve tissue. If the valve is damaged, it must be replaced!
- Do not attempt to eliminate any defects of the valve! The damaged valve must not be used!
- Do not use unprotected forceps or sharp instruments, since they may cause structural damage to the valve.
- Use caution when tying knots to avoid deformation and damage of valve stent posts.
- Never handle the valve leaflets.
- Avoid prolonged contact with the storage solution. Immediately after contact, thoroughly flush any skin exposed to the solution with water. In case of contact with eyes, flush with water and seek appropriate medical care.

MRI Safety Information
Clinical studies showed that the valve can be safely scanned under the following conditions:
- Static magnetic field of 3 Tesla or less
- Spatial gradient of 525 Gauss/cm or less
- Maximum whole-body-averaged specific absorption rate (SAR) of 2.0 W/kg for 15 minutes of scanning

Pre-clinical trials demonstrated that the UniLine valve produced a maximum temperature rise of less than 0.5°C when exposed to a maximum whole-body-averaged SAR of 2.0 W/kg for 15 minutes of continuous scanning in a 3-tesla MR system. MR image quality may be compromised if the area of interest is relatively close to the position of the bioprosthesis.

ADVERSE EVENTS

From 2011 to 2020, four thousand seven hundred ninety-five (4795) UniLine aortic valves were implanted. The results of UniLine clinical study proves its safety.
Adverse events potentially associated with the use of bioprosthetic heart valves include:
- Hemolysis
- Hemolytic anemia
- Stroke
- Myocardial infarction
- Hemorrhage
- Cardiac arrhythmia
- Regurgitation, paravalvular or transvalvular
- Heart failure
- Angina
- Structural deterioration (primary tissue failure with/without calcification, leading to the change in the leaflet morphology, leaflet deformation, perforation, tear, or other)
- Valve thrombosis
- Valve stenosis
- Thromboembolism
- Endocarditis

It is possible that these complications could lead to:
- Reoperation
- Persistent disability
- Death

CLINICAL STUDIES

The first results of evaluation of short-term clinical and functional results of UniLine aortic valve placement were obtained in 2011. From November 2011 to March 2013, the aortic valves were replaced by UniLine bioprostheses in 29 patients in the clinic of the Scientific Research Institute for Complex Issues of Cardiovascular Diseases of the Siberian Branch of the Russian Academy of Medical Sciences, Kemerovo, and 43 patients in the clinic of the National Medical Research Center for Circulation Pathology n.a. Academician E.N. Meshalkin, Novosibirsk. Thus, a total of 72 patients (32 men and 40 women) were operated. The average age of patients was 68.6±5.2 years. A majority of patients had a degenerative disease (76%), which resulted in the prevalence of stenosis (86%) when compared to other anatomical variants. The average NYHA functional class was 2.84±0.31. The effective orifice area (EOA) of the aortic valve affected was, as a rule, not more than 1.0 cm^2 with a mean of 0.74±0.20 cm^2. EOA indexed for the body surface area was 0.36±0.09 cm^2/m^2. The peak pressure gradient showed a mean rise up to 89.7±24.4 mm Hg with a mean gradient of up to 56.0±13.4 mm Hg. Prior to the surgery and prior to discharge (on average, 19 days after the surgery) all patients underwent echocardiography to check the function of the aortic valve prosthesis and left ventricle (using Vivid 7, GE Healthcare, and IE 33, PHILIPS systems). The valve prosthesis function was evaluated by EOA. The report on the evaluation of performance characteristics of UniLine bioprostheses was updated with results of tests of each valve in the pulsatile flow bench described by the manufacturer in the individual functional data sheet included in the bioprosthesis scope of delivery (see Table 2). The following specifications were considered: the maximum orifice area (S_{max}, cm^2) calculated planimetrically, flow rate (volume per minute, L/min) at a pulse rate of 70 per minute. The function of the left ventricle (LV) was assessed by linear and volumetric dimensions during systole and diastole: left ventricular end-diastolic dimension (LVEDD) and volume (LVEDV), end-systolic dimension (LVESD) and volume (LVESV). In addition, end-diastolic values were indexed for the body surface area. The LV contractility was assessed using ejection fraction (EF) and shortening fraction (SF) values. The grade of myocardial hypertrophy severity was determined by the LV myocardial mass and LV myocardial mass index. The statistical analysis was performed with Statistica 10.0 software. Mean values and standard deviations were calculated for most parameters. The Kolmogorov–Smirnov nonparametric test was used to evaluate intergroup differences. Study results are shown in Tables 3 and 4.

PACKAGING AND STORAGE
The valve is supplied with the holder attached to it with three retaining sutures. The holder is intended to facilitate the treatment and handling when removing the valve from the container, and during rinse and implantation.
The valve is stored in a 0.3% paraben mix solution..
Store the valve in the vertical position.

CAUTION: Do not implant the valve without thoroughly rinsing as directed in the instructions for use.
WARNING: Do not use the valve if the temperature indicator has changed its color, or if the valve has been improperly stored in temperature conditions outside of the +5°C to +40°C range.

INSTRUCTIONS FOR USE
Read the UniLine Instructions for Use which contain specific guidances for cleaning and placement.
WARNING: The valve size depends on the size of the recipient annulus and anatomical features of the sinotubular junction. Implantation of the valve with a size larger than that of the annulus is not recommended, as it may result in stent deformation, valvular incompetence, and/or damage to the surrounding tissues. Do not use inappropriately large valves! The valve dimensions are presented in Table 4. Perform preoperative echocardiography to select an optimal valve size.

Preimplant Handling
UniLine valve is supplied in a container with a tamper-evident film. The contents of the container are sterile; the container itself requires aseptic treatment before being placed into the sterile field to prevent contamination.
Warnings
- Do not use the valve if the expiration date has elapsed.
- Do not use the valve if the fluid is leaking from the packaging.
- Do not resterilize the valve by any method.

Valve Removal from the Carton
Precautions
- Do not place the non-sterile valve storage container in the sterile field.
- Do not expose the valve to solutions other than the storage solution in which it is supplied by the manufacturer. The sterile saline is used to rinse and irrigate the valve.
- Do not add antibiotics to either the valve storage solution or the rinse solution.
- Do not apply antibiotics to the valve.

1. The surgeon selects the correctly sized valve.
2. After you remove the valve storage container from the carton, examine it for signs of damage.

WARNING: Do not use the valve if the tamper-evident film is damaged, broken, or missing, or if fluid is leaking from the packaging.

WARNING: Do not use the valve if you discover that it is not completely covered by the storage solution.
3. Check the valve size and expiration date indicated on the film.
4. To remove the valve from the storage container, take off in the tamper-evident film and unscrew the lid.
CAUTION: Avoid prolonged contact with the storage solution. Immediately after contact, thoroughly flush any skin exposed to the solution with water. In case of contact with eyes, flush with water and seek appropriate medical care.

Valve Removal from the Storage Container
1. Prepare the holder handle.
2. Screw the handle into the holder fixed to the valve as shown in Figure 2.
3. Remove the valve and the protective plastic glass from the storage container.
CAUTION: Do not use unprotected forceps or sharp instruments, since they may cause structural damage to the valve.
CAUTION: Never handle the valve leaflets.
4. Put on the gloves and remove the valve from the protective plastic glass as shown in Figure 3.
5. Check the valve for damage. DO NOT implant the valve if there are any signs of damage or defects.

Rinse Procedure
CAUTION: Do not implant the UniLine valve without thoroughly rinsing.
1. Prepare two basins in the sterile field and fill each of them with not less than 500 mL of the sterile saline.
2. Using the holder handle, fully immerse the valve, the holder, and the portion of the holder handle in the sterile saline in the first basin as shown in Figure 4.
3. Rinse the valve for two minutes, using a gentle back-and-forth motion.
4. Repeat Steps 2 and 3 in the second basin.

5. After rinsing, leave the valve immersed in the second basin until required

for implantation by the surgeon.

CAUTION: Do not allow the valve tissue to dry. Place the valve in the saline immediately upon removal from the storage solution. During implantation, the valve must be periodically irrigated with the saline.

Surgical Guidelines

Due to the complexity of the surgical procedure for replacement of the valve, the choice of the implantation technique, as well as pre- and postoperative treatment is left to the discretion of the individual surgeon with account of these instructions.

When implanting in the supra-annular position, it is not recommended to use the mattress suture.

Make sure the suture material is not in the contact with the leaflets.

Precautions

• Do not allow the valve tissue to dry. Place the valve in the sterile saline rinse solution immediately upon removal from the valve storage solution. The valve must be periodically irrigated during implantation.

• Use caution during suturing though the cuff to avoid laceration of the valve tissue. If the valve is damaged, it must be replaced.

• Do not attempt to eliminate any defects of the valve! The damaged valve must not be used!

VALVE IMPLANTATION

To obtain the optimal hemodynamic results, the valve should be implanted in the supra-annular position.

1. Choose the appropriately sized valve. Make sure the suture material is not in the contact with the leaflets and posts.

WARNING: Position the valve so that the stent does not obstruct the coronary ostia.

2. To remove the holder from the valve: cut three retaining sutures as shown in Figure 5 and pull the handle.

3. After removing the holder, make sure that there are no residual threads by which the holder was retained.

INTRAOPERATIVE ASSESSMENT

It is recommended to perform the intraoperative assessment of the valve function with transesophageal Doppler echocardiography.

PATIENT REGISTRATION

Each valve is supplied with the Implantation registration form

, identification sticker for the medical record and a mail envelope to be sent to the manufacturer.

Please, fill in the Implantation registration form after implantation and send it to NeoCor CJSC.

Control by the manufacturer is mandatory in some countries. Disregard any request for patient information if this contradicts your local legal or regulatory requirements regarding patient personal data.

POSTOPERATIVE CARE

Anticoagulant and/or Antiplatelet Therapy

As a rule, it is recommended to maintain patients with the biological heart valve prosthesis on the anticoagulant therapy for 24 weeks after implantation.

Long-term anticoagulant therapy, unless contraindicated, is recommended for all patients with biological heart valve prosthesis who have risk factors for thromboembolism.

If prosthetic dysfunction develops in the long term, the decision can be made, based on results of the medical examination, to remove and replace the valve.

PATIENT COUNSELING INFORMATION

Long-term anticoagulant therapy, unless contraindicated, is recommended for all patients with bioprosthesis who have risk factors for thromboembolism.

Prophylactic antibiotic treatment is recommended in invasive procedures (tooth extraction, cavity probing, etc.).

SHIPPING, STORAGE, AND DISPOSAL

The UniLine valve packed in the shipping container is shipped in the covered vehicles at +5°C to +40°C by any transport. The carton contains the temperature indicator triggering in case of the inappropriate temperature range of shipping and storage. Used valves can be handled and disposed of as medical waste and biohazardous materials. There are no special risks related to the disposal of the UniLine valve.

WARRANTY

NeoCor CJSC guarantees that the UniLine valve complies with Technical Specifications (TU) 9444-010-57628698-2008 provided that these instructions for use, and the condition of shipping, and storage are followed. THIS WARRANTY IS IN LIEU OF AND EXCLUDES ANY OTHER WARRANTIES NOT EXPRESSLY SET FORTH HEREIN, EXPRESS OR IMPLIED BY OPERATION OF LAW OR OTHERWISE INCLUDING, BUT NOT LIMITED TO, ANY IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, since treatment, storage, rinse, sterility of this device, as well as the patient-related factors such as diagnostics, treatment, surgical procedure and other concerns that are beyond NeoCor CJSC control directly impact the device and results of its use. NeoCor CJSC SHALL NOT BE LIABLE FOR ANY INCIDENTAL OR CONSEQUENTIAL LOSS, DAMAGE OR EXPENSE, directly or indirectly arising from the use of this device other than the replacement of all or part of it. NeoCor CJSC neither assumes nor authorizes any other person to assume for it any other additional liabilities related to this device.

This limited warranty grants you certain legal rights. You may have other rights that vary depending on the jurisdiction.

Description of specifications appearing in the documents of NeoCor CJSC are meant solely to generally describe the device during manufacturing and do not constitute any additional warranties.

Table 1: Valve Dimensions

Bore diameter (size), mm	Outer Diameter, mm	Aortic Protrusion, mm	Height, mm
21±1	23±1	10.5±1.5	14.5±1.5
23±1	22±1	11.5±1.5	15.5±1.5
25±1	27±1	12.5±1.5	16.5±1.5

Table 2: UniLine Performance Specifications Established in the Course of Bench Tests (Manufacturer's Data)

Parameter	**Bore diameter (size), mm**		
	21	**23**	**25**
Flow rate (minimum volume), cm^3/cycle	90±3	96±6	108±10
Regurgitation, cm^3/cycle	3.027±1.19	2.98±0.63	3.73±0.89

Table 3: Hemodynamic Properties of UniLine Aortic Bioprostheses Depending on the Prosthesis Diameter

Parameter	**Bore diameter (size), mm**		
	21	**23**	**25**
EOA (cm^2), min–max	1.79±0.2 1.77–1.81	1.97±0.09 1.88–2.06	2.07±0.10 1.97–2.17
ΔP_{peak}, mm Hg, min–max	18.1±5.3 8–31	17.9±5.0 9–33	18.4±6.2 6–32
ΔP_{mean}, mm Hg, min–max	13.8±4.1 6–27	10.0±3.6 4.6–30	8.0±3.1 3.8–13

Note: EOA, effective orifice area; ΔP_{max}, maximum gradient of the aortic valve; ΔP_{mean}, mean gradient of the aortic valve. Mean values are specified in the upper line, minimum and maximum values are specified in the lower line.

Table 4: Changes of LV Functional Parameters after Surgery

Parameter	**Pre-surgery**	**Post-surgery**	**P_{1-2}**
LVEDV, mL	125.9±49.7	111.4±32.9	0.42
End-diastolic volume index, mL/m^2	67.9±26.0	63.4±19.4	0.67
LVEDD, cm	4.98±0.83	4.82±0.5	0.55
End-diastolic dimension index, cm/m^2	2.64±0.51	2.51±0.49	0.62
LVESV, mL	48.9±24.9	44.4±18.5	0.34
LVESD, cm	3.17±0.68	3.23±0.50	0.83
LV ejection fraction, %	63.5±9.3	61.4±7.0	0.38
LV shortening fraction, %	36.0±7.4	32.8±5.8	0.78
LV myocardial mass, g	358.9±80.3	336.0±57.3	0.20
LV myocardial mass index, g/m^2	202.5±47.4	186.4±39.5	0.37
Cardiac index, $L/min/m^2$	4297.9±873.8	3673.7±911.4	0.89

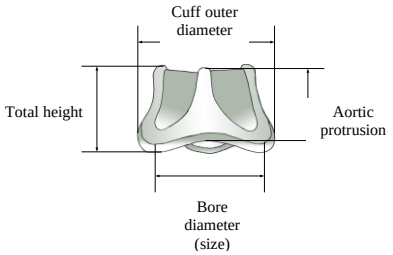

Figure 1: UniLine Aortic Valve

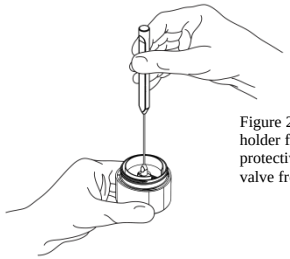

Figure 2: Screw the handle into the holder fixed to the valve, remove the protective plastic glass containing the valve from the carton.

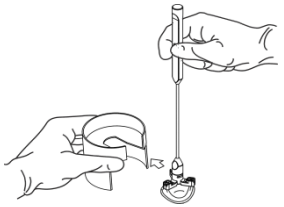

Figure 3: Remove the valve from the protective plastic glass.

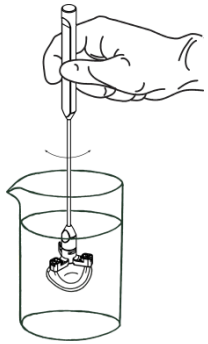

Figure 4: Rinse the valve in the sterile saline for 4 minutes, changing the saline twice (every 2 minutes).

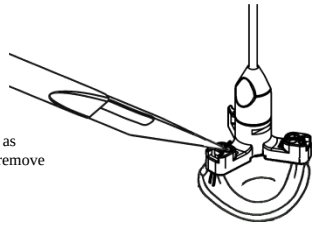

Figure 5: CAUTION!
Cut the retaining sutures as shown in the figure and remove the holder.

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