Summary of Safety and Clinical Performance

RP-602000-001

Version B

02 December 2024

Summary of Safety and Clinical Performance

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

1.1 Device Trade Name	NeoChord DS1000 NeoChord DS1000 Artificial Chordae Delivery System
1.2 Manufacturer's Name and address	NeoChord, Inc. 10900 73rd Ave N., Suite 101, Maple Grove, MN 55369, USA
1.3 Manufacturer Single Registration Number (SRN)	US-MF-000008440
1.4 Basic UDI-DI	The device Unique Device Identification (UDI) as in EUDAMED is 08666540001500000-002C9.
1.5 Medical Device Nomenclature Description/Text	The Global Medical Device Nomenclature (GMDN) code of NeoChord DS1000 is 60653. The European Medical Device Nomenclature (EMDN) code of NeoChord DS1000 is C03900299.
1.6 Class of the Device	Class III
1.7 Year when the First Certification (CE) was Issued Covering the Device	December 2012
1.8 Authorized Representative Name and SRN	MPS Medical Product Service GmbH Borngasse 20, 35619 Braunfels, Germany
1.9 Notified Body (NB) Name and Single Identification Number	BSI Group The Netherlands B.V. NB 2797

2. Intended Use of the Device

2.1 Intended Purpose	Repair of chordal elongation and rupture resulting in mitral valve prolapse.
2.2 Indication(s) and target populations(s)	Indicated for use in patients with Grade 3+ or 4+ mitral valve regurgitation who are candidates for surgical mitral valve repair or replacement.
2.3 Contraindications and/or limitations	• Heavily calcified valves • Valvular retraction with severely reduced mobility • Active bacterial endocarditis • Complex mechanism of MR (leaflet perforation, etc.) • Significant tethering of leaflets • Inflammatory valve disease CAUTION: The NeoChord DS1000 has not been studied in patients with functional mitral regurgitation. CAUTION: The NeoChord DS1000 has not been studied in patients with anterior leaflet prolapse.

	WARNING: Patients who exhibit evidence of fragile tissue (e.g., severely dilated left ventricle, cachexia) may not be appropriate candidates for this surgery.

3. Device Description

3.1. Description of the device

The NeoChord DS1000 (**Figure 1**) is a single-use, hand-held device designed to deploy artificial chordae through a minimally invasive incision that accesses the mitral valve through the left ventricle while the heart is beating. The DS1000 deploys artificial chordae using commercially available expanded polytetrafluoroethylene (ePTFE) suture material, labeled for use as artificial chordae tendineae. The NeoChord DS1000 is an integrated modular system consisting of a hand-held delivery instrument, a cartridge in which ePTFE suture is loaded, a needle, and a tethered Leaflet Capture Verification monitor (LCV) that enables confirmation of capture of the free edge of the mitral leaflet in the distal clamp of the delivery instrument prior to deploying the ePTFE suture and knot at the leaflet.

The system is sterilized using Ethylene Oxide and is supplied sterile in disposable packaging.

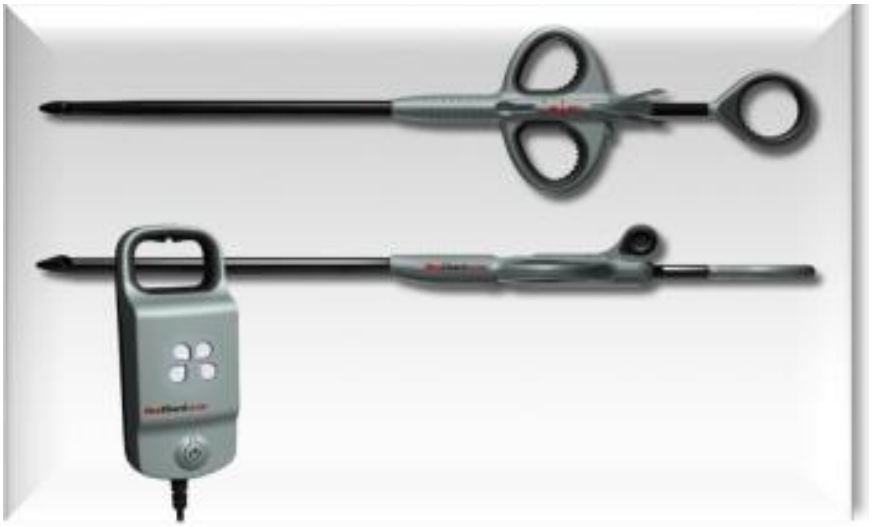

FIGURE 1. NEOCHORD DS1000

The NeoChord DS1000 provides a minimally invasive alternative to the conventional surgical approach for mitral valve repair with artificial neochordae (which includes stopping the heart and cardiopulmonary bypass). The device trans-apically accesses the mitral valve, grasps the flailing or prolapsing leaflet, and deploys a suture as an artificial chord via a limited left lateral thoracotomy in a beating heart. The device is a battery-powered, hand-held delivery instrument which consists of the following components (**Figure 2**)

- Leaflet Capture Verification (LCV) Monitor
- Fiber Optic Cable
- Multi-Use Needles

- Reloadable Suture Cartridges
- Delivery Instrument

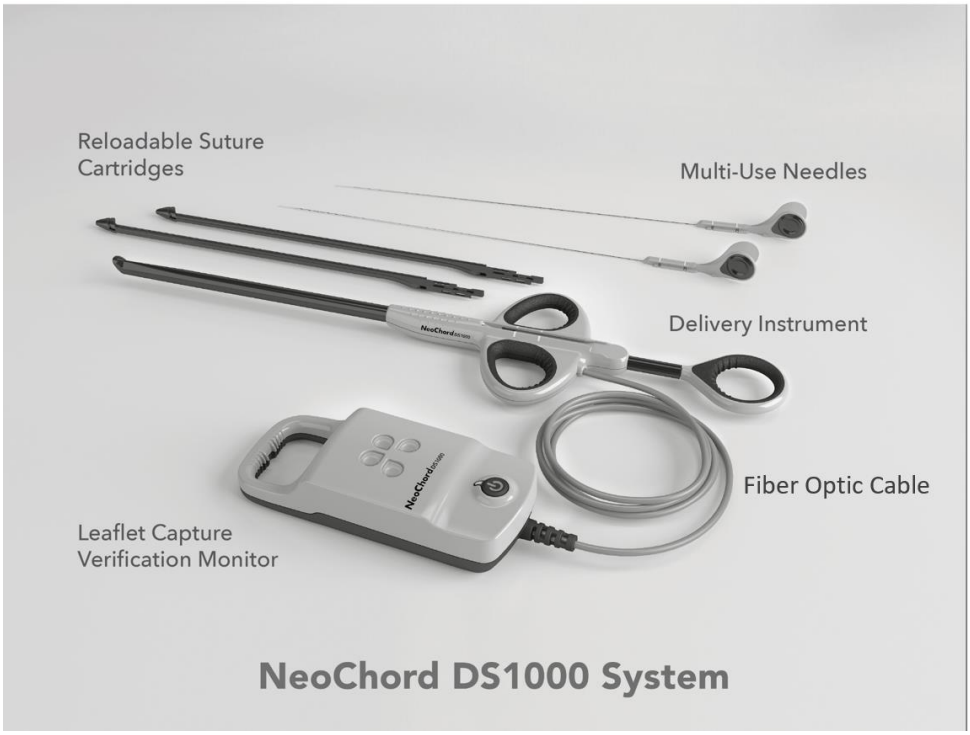

FIGURE 2. NEOCHORD DS1000 COMPONENTS

The table below (**Table 1**) provides an overview of the products available for NeoChord DS1000.

TABLE 1. LIST OF PRODUCTS AVAILABLE FOR NEOCHORD DS1000

Catalogue Number	Description
500000-002	NeoChord DS1000

3.2. Generations or Variants of Device

There are no previous generations or variants of the device.

3.3. Replaceable Components or Accessories

The DS1000 does not have any replaceable components or accessories.

3.4. Products Intended to be Used in Combination with Device

Commercially available ePTFE suture indicated for chordae tendinae repair or replacement with a mean diameter of 0.307mm (e.g. GORE™ CV-4) or 0.246mm (e.g. GORE™ CV-5)

4. Information on Residual Risks and Any Undesirable Effects, Warnings and Precautions

4.1. Residual risks and undesirable effects

A Residual Risk / Benefit Analysis has been performed for the NeoChord DS1000. All residual risks following the implementation of mitigations were evaluated. The overall and individual risk-benefit analyses concluded that the clinical benefits of the products outweigh the residual risk, also in relation to the state of the art. Therefore, the residual risk of the NeoChord DS1000 is considered acceptable.

The potential risks associated with the use of the NeoChord DS1000 System include the following:

- Air embolism
- Allergic reaction
- Arrhythmias
- Bleeding (with or without requiring transfusion)
- Broken ribs
- Conversion to standard valve repair surgery
- Damage to cardiovascular or nervous tissue
- Infection
- Failure to deliver ePTFE artificial chord to intended leaflet site
- Mitral regurgitation (>3)
- Mitral valve injury
- Pericardial damage
- Peripheral embolism
- Pulmonary embolism
- Stroke (cerebrovascular accident) or transient ischemic attack

The potential risks associated with the general cardiac surgery include the following:

- Angina
- Allergic reaction (anesthetic)
- Cardiac arrest
- Cardiac perforation
- Cardiac tamponade
- Death
- Dilation of heart
- Drug reactions to antiplatelet / anticoagulation agents / contrast media
- Emergency cardiac surgery
- Endocarditis
- Heart Failure
- Hemolysis
- Hematoma
- Hypertension / hypotension
- Mitral stenosis

- Myocardial infarction
- Outflow tract obstruction
- Prolonged ventilation time
- Renal compromise
- Re-operation
- Septicemia
- Thrombosis
- Wound dehiscence

4.2. Warnings and precautions

Warnings:

- Use of the NeoChord DS1000 should be limited to physicians that have received training on the use of the device.
- Use of the device requires a minimum of one trained physician / operator and one trained member of the operating room staff.
- The NeoChord DS1000 is sterilized using EtO and is for single use only. Do not reuse or resterilize. Attempts to reuse or resterilize the device may result in patient harm, device malfunction, or inadequate sterilization.
- To avoid serious eye injury do not look directly into LED lumens at distal tip of the device.
- The NeoChord DS1000 is not suitable for use in the presence of flammable anesthetic
- mixture with air, oxygen nor nitrous oxide.
- The NeoChord DS1000 is not defibrillation proof and must be removed from the patient if defibrillation of the heart is required.
- The NeoChord DS1000 is not designed, nor should an attempt be made, to connect the system with any endoscopic devices.
- To minimize risks associated with the use of electrically powered devices during surgical procedures, ensure all devices are conformant with the relevant IEC and ISO standards and that their use is in accordance with Clause 16 of IEC 60601.
- Do not attempt to tether the Leaflet Capture Verification monitor onto any high voltage devices within the operating room.
- After use of the NeoChord DS1000, dispose of all elements of the device, including cartridges, needles, and Leaflet Capture Verification monitor in accordance with accepted institutional practice and in compliance with applicable laws and regulations including those pertaining to biohazardous material, needles, and device batteries.
- No modifications of this equipment are allowed.

Precautions:

- The NeoChord DS1000 should be used in accordance with the necessary safety precautions appropriate to a thoracic device implantation procedure.
- Inspect package prior to use. Do not use any component of the system if damage to the sterile package is noted. Inspect all components prior to use. Do not use damaged, expired, or non-sterile components.
- Do not use a device that has been dropped from a height of greater than eighteen (18) inches.
- The NeoChord DS1000 is to be used with ePTFE suture material that has an indication for use to repair or replace native chordae tendineae and which have a mean diameter of 0.307mm (e.g., GORE™ CV-4) or 0.246mm (e.g., GORE™ CV-5) only. Do not use the DS1000 with other suture materials or sizes as the compatibility of the DS1000 with other suture material and sizes is not known.

4.3. Other relevant aspects of safety

Corrective actions:

- No safety related corrective actions.

5. Summary of Clinical Evaluation and Post-market Clinical Follow-up (PMCF)

5.1. Summary of clinical data related to equivalent device – no equivalent device is available.

5.2. Summary of clinical data from conducted investigations of the device before the CE-marking. (Pre-Market Clinical Data)

One pre-market clinical study (NCT01777815, RP-610404-102) was conducted to support the original CE Mark and provided information about how the device should be used and on which patients it was most effective.

Title: Safety and Performance Study of the NeoChord Suturing Device in Subjects With Degenerative Mitral Valve Disease; Diagnosed With Severe Mitral Regurgitation (TACT Trial)

Summary: The primary objective of the study was to validate performance and substantiate claims that suture deployment with the NeoChord DS1000 in a beating heart can be done safely, that surgeons are able to successfully gain access to the mitral leaflets using TEE visualization, and that the instrument performs as intended.

The study was a multicenter, prospective, single-arm, open-label study conducted at centers in Denmark, Germany, Italy and Lithuania.

A total of 30 subjects were enrolled. After the first patient was implanted, the recommendation was made to all centers to implant at least two neochords during the procedure instead of just one. The first 15 patients in this cohort were implanted using a mid-line apical access. The next

15 patients were implanted using a postero-lateral apical access, which led to better results. All 30 patients were followed for 2 years.

The NeoChord DS1000 System reliably placed the neochordae sutures, showing an 86.7% acute procedure success rate in the overall cohort, and a 100% acute procedure success rate in the cohort of patients who underwent the procedure after the access was modified. The 30-day performance improved with the procedural modification, with 58.6% of patients in the overall cohort maintaining a ≤2+ mitral regurgitation Grade, and with the procedural modifications, 85.7% maintaining a ≤2+ mitral regurgitation Grade. The 1-year results are consistent with the experience of comparable procedures on the market.

The safety profile improved throughout the course of the study, with 8 (26.7%) patients experiencing a major AE within 30 days in the overall cohort (death (n=1), reoperation for failed repair (n=6), procedure-related blood transfusion >2 units (n=5), procedural ventilation >48h (n=1), stroke (n=1)), and 1 (6.7%) patient experiencing a major AE within 30 days in the Posterolateral Cohort. A similar profile was observed after the 30-day visit with 6 (20%) patients experiencing a major AE, including 2 (13.3%) in the posterolateral cohort. Since most of the major AEs occurred in patients who had a failed implant and, therefore, required a prolonged procedure or a reoperation, the safety profile improved with the changes to the surgical procedure.

5.3. Summary of Clinical Data from Other Sources

5.3.1. Device literature

A comprehensive literature search was conducted to identify clinical performance and clinical safety data not held by the manufacturer. The literature review is based on evidence from the DS1000 device only. In total, 21 articles which reported clinical performance and/or safety outcomes were included in the literature review for the NeoChord DS1000 [1-21], covering the period between December 2013 and September 2024. These studies included 1,290 patients in total. On average (median), the age of the patients was 64 years, and the majority of patients (72%) were males. All studies were restricted to primary (i.e., degenerative) MR. The majority of patients had severe MR (grade 3+ or 4+) at the time of inclusion. The mean follow-up time after the procedure was 12 months. More details are provided in **Table 2**.

TABLE 2. DEVICE LITERATURE - STUDY CHARACTERISTICS

Characteristic	**Median [IQR] (Range) / Classification**
Sample size	52 [18 - 90] (range: 6-213)
Mean age (years)	64 [60 - 66] (range: 50-78)
Male (%)	72 [68 - 78] (range: 29-94)
Mean follow-up (months)	12 [6 - 24] (range: 1-60)
MR Characteristics	
Type of mitral regurgitation	Primary (i.e., degenerative)
Severity of MR at inclusion (number of references)	Severe (n=17), Advanced (n=1), Not Reported (n=1)

5.3.1.1. Performance outcomes

Clinical data were included involving the intended indication of NeoChord DS1000. Discussed endpoints include: Technical success rate, device success rate, procedural success rate, patient success rate, acceptable MR reduction, absence or trivial MR, and re-operation. The details are shown in **Table 3**.

TABLE 3: DEVICE LITERATURE - PERFORMANCE OUTCOMES

Performance Endpoint	Number of references	Median [IQR]	Range
Technical success rate (%)	13	99% [97 100]	83%-100%
Device success rate (%)			
1 month	2	93% [90 97]	86%-100%
6 months	3	81% [79 85]	77%-88%
1 year	3	84% [78 91]	72%-99%
2 years	1	59% [NA]	NA
3 years	1	49% [NA]	NA
Procedural success rate (%)			
6 months	2	100% [NA]	NA
1 year	2	92% [90-93]	89%-94%
Patient success rate (%)			
6 months	2	94% [NA]	88%-100%
1 year	3	91% [88 92]	84%-92%
2 years	2	87% [85 88]	84%-90%
3 years	1	81% [NA]	NA
Acceptable MR reduction (MR ≤2+) (%)			
Direct after leaving OR	9	100% [99 100]	97%-100%
Discharge	10	99% [93 100]	75%-100%
1 month	9	93% [88 97]	75%-100%
2 months	1	100% [NA]	NA
3 months	3	99% [98 100]	97%-100%
6 months	8	99% [92-99]	72%-100%
1 year	10	94% [91 98]	86%-100%
2 years	5	97% [95 100]	80%-100%
2.5 years	1	79% [NA]	NA
3 years	2	87% [83 90]	79%-94%
5 years	1	100% [NA]	NA
MR absence / trivial MR (%)			
direct after leaving OR	6	63% [56 792]	55%-100%
discharge	8	41% [33 42]	31%-100%
1 month	7	42% [37 44]	33%-46%
2 months	1	47% [NA]	NA
3 months	3	45% [45 73]	44%-100%
6 months	7	36% [35 37]	14%-100%
1 year	7	31% [30 37]	27%-100%
2 years	3	31% [26 41]	20%-50%

Performance Endpoint	Number of references	Median [IQR]	Range
2.5 years	1	33% [NA]	NA
3 years	1	12% [NA]	NA
Reintervention (%)			
1 month	3	2% [1 8]	0%-13%
6 months	4	5% [2 8]	0%-13%
1 year	6	5% [3 7]	0%-13%
2 years	2	10% [5 15]	0%-20%
3 years	2	15% [7 22]	0%-29%
within 3 months	3	6% [3 11]	0%-16%
within 6 months	3	0% [0 6]	0%-11%
within 2.5 years	2	6% [3 9]	0%-13%
any time until end of observation	10	7% [5 13]	0%-32%
Conversion to open repair (%)	13	1% [1 4]	0%-17%

5.3.1.2. Safety outcomes

The table below provides the median of safety outcomes the adverse event rates reported by a consensus document from the Mitral Valve Academic Research Consortium published in the Journal of the American College of Cardiology [18]. See **Table 4** for more details, including the number of references per safety outcome.

TABLE 4. ADVERSE EVENT RATES OBSERVED IN DEVICE LITERATURE

Safety Endpoint	Number of references	Median [IQR]/text	Range
Mortality rate (%)			
Any time until end of observation	16	0.7% [0 2.6]	0%-6.7%
<30 days post-procedure	18	0.4% [0 1.4]	0%-6.0%
>30 days post-procedure	12	0.0% [0 0.09]	0%-6.7%
Hospitalization (%)	5	0% [0 0]	0%-0%
Neurological events (%)	15	0% [0 0.3]	0%-10%
Myocardial infarction (%)	13	0% [0 0.5]	0%-2.0%
Access and vascular complications (%)	11	0% [0 0.5]	0%-5.0%
Bleeding complications (%)			
Any blood transfusion	10	1.3% [0 7]	0%-15.0%
Minor (1-2 blood units transfused)	10	0% [0 7.1]	0%-29.0%
Major (3 blood units transfused)	11	0% [0 1.4]	0%-3.9%
Extensive (4 or more blood units transfused)	10	0% [0 0.6]	0%-4.0%
Life-threatening (surgical intervention needed)	8	0% [0 0]	0%-1.4%
Acute kidney injury	13	2.6% [0 8.9]	0%-14.0%
Newly onset arrythmias or conduction system disturbances (%)	15	22.5% [12.0-26.8]	0%-41.2%
Device related AE or technical failure	3	Minor pericardial effusion (average rate 5.7%)	2.6%-8.5%

5.3.1.3. Summary Performance and Safety Outcomes

In total, 10 prospective studies, 6 retrospective studies, 2 studies that are following up on the TACT trial and 3 case series were included that supported the safety and performance of the subject device and contribute useful data in terms of the risks and benefits associated with treatment.

Overall, the NeoChord DS1000 has been well-studied in multiple studies that measured the performance and safety of the device using outcome measures that are also used in the state of the art.

5.3.2. PMS data - Complaints

Between 01 January 2019 and 27 September 2024, a total of 59 complaints were reported (**Table 5**). Most reported complaint events by failure mode were: Suture pulled off leaflet (n=13), needle unable to load (n=8), and post-procedure MR returned (n=4) . Five complaints have been made that are pending receipt of the device to complete the investigation. None of these complaints were reportable.

TABLE 5. COMPLAINTS PER TYPE PER YEAR

Complaint Failure Mode	2019	2020	2021	2022	2023	2024 [1]	Total
Cartridge loading difficulty	1	1	0	1	0	0	3
Cartridge loading difficulty – User Error	0	0	0	0	0	1	1
Device jaw failed to close	0	2	0	0	0	0	2
Device handle separation	0	0	0	0	1	1	2
Intra-operative bleeding	1	0	0	0	0	0	1
LCV Monitor Lights not working	0	0	1	0	0	0	1
Loose chords	1	1	0	0	0	0	2
Native chord rupture	1	0	0	0	0	0	1
Needle did not capture suture	0	0	0	1	0	1	2
Needle difficult to advance	1	0	0	0	0	0	1
Needle unable to load	1	4	3	0	0	0	8
Post-procedure MR returned	1	3	0	0	0	0	4
Reduction of loss of LCV monitor functionality and visual feedback	0	0	0	0	0	2	2
Suture pulled off leaflet	3	3	4	2	1	0	13
Suture rupture	1	1	1	0	0	1	4

Complaint Failure Mode	2019	2020	2021	2022	2023	2024 [1]	Total
Suture sticking in device	1	0	0	0	0	0	1
Tear created in left atrium	0	2	0	0	0	0	2
Thumb ring did not push smoothly after the suture was loaded	0	0	1	0	0	0	1
Part of the left atrium was grasped with the leaflet	1	0	0	0	0	0	1
Patient alleges breast implant rupture related to procedure	1	0	0	0	0	0	1
Pending investigation	0	0	0	0	0	5	5
Total	14	17	10	4	0	6	59

[1] Until 01 September 2024

5.3.3. Medical device registries

Searches in regulatory databases were performed for the period 01 January 2018 to 01 March 2023 to identify any additional safety events or complaints. There were no complaints reported in any database for the NeoChord DS1000 (**Table 6**).

TABLE 6. COMPLAINTS FOUND IN REGULATORY DATABASES

Database	Number of hits
Canadian Federal Database of Safety Alerts and Recalls (Canada)	0
MHRA Medical Device Alerts (UK)	0
SwissMedic Recalls & FSCA (Switzerland)	0
Federal Institute for Drugs and Medical Devices (BfArM) (Germany)	0
Health Products Regulatory Authority (Ireland)	0
ANSM (France)	0

5.4. Overall summary of the clinical safety and performance

5.4.1. Safety analysis

The *overall mortality rate <30 days* when using the NeoChord DS1000 ranges from 0-6.7% (median: 0.5%), which is in line with the mortality rates reported in the state-of-the-art literature (range 0-6.1%; median: 1.3%). The *overall mortality rate >30 days* when using the NeoChord DS1000 ranges from 0-6.7% (median: 0%), while the state-of-the-art reports a range between 1.6% and 18% (median: 7.7%). From this, it was concluded that the overall mortality rate when using the NeoChord DS1000 is acceptable compared to the state-of-the-art.

Hospitalization rate was not reported in NeoChord DS1000 studies (0% in 5 studies), while the state-of-the-art reports a median of 18.0% (range: 6.3-35.5%), implicating that Neochord performs superior for this safety endpoint.

The *neurological events* rate ranges between 0% and 10% (median: 0%) when using NeoChord DS1000, which is in line with the range reported in the state-of-the-art (0.6%-7.7%; median: 1.6%). *Myocardial infarction* rate is low when using NeoChord DS1000 (median 0%, range 0%-2.0%), as was the case in the state-of-the-art (median 0%, range 0%-7.7%). *Access and vascular complication* rates are comparable when using NeoChord DS1000 (median 0%, range 0%-5.0%) or alternative treatments (median 0%, range 0%-3.8%). *Bleeding complications* are comparable (NeoChord: median 3.5% (range: 0%-15%); alternative treatments: median 3.3% (range: 0-13%). *Acute kidney injury* was somewhat more frequently observed when using the NeoChord DS1000 (median 2.6%, range 0%-14.0%) compared to alternative treatments (median 0.8%, range 0%-9.6%).

Taken together, the NeoChord DS1000 is a safe device, as it performed comparable or sometimes even superior compared with the state-of-the-art treatments on almost all safety endpoints.

5.4.2. Performance analysis

The NeoChord DS1000 is intended to repair chordal elongation and rupture resulting in mitral valve prolapse, which in turn leads to mitral valve regurgitation. The clinical evaluation reviewed results of the clinical investigations and literature with the NeoChord DS1000, that were obtained under conditions consistent with the intended purpose of the device. The device literature showed sufficient data to confirm that mitral valve repair using the NeoChord DS1000 results in reduction of MR and thereby achieved its performance objective. Device literature showed high technical success rates (99%, range: 83%-100%), device success rates (93%, range: 86%-100%), and procedural success rates (92%, range: 89-94%). These rates are acceptable when compared to performance rates reported for alternative treatments in the state-of-the-art, which showed a technical success rate of 97%, a device success rate of 85% and a procedural success rate of 91%.

In conclusion, the evidence presented in this clinical evaluation sufficiently demonstrates that the NeoChord DS1000 achieves the intended performance objective. The performance objective of the evaluation is therefore considered to be met and conformity of the NeoChord DS1000 with the requirement on clinical performance (**GSPR 1**) has been demonstrated.

5.5. Ongoing or Planned Post-Market Clinical Follow-up

As part of the PMCF Plan, the following clinical investigations are currently ongoing or have been completed (**Table 7**):

TABLE 7. POST-MARKET CLINICAL FOLLOW-UP STUDIES - INITIATED BY THE MANUFACTURER

Device	ClinicalTrials.gov Identifier	Study Title	Short Title	Status
NeoChord DS1000	NCT01784055	NeoChord TACT Post-Market Surveillance Registry	TACT registry	Completed
NeoChord DS1000	NCT02803957	Randomized Trial of the Neochord DS1000 System Versus Open Surgical Repair	ReChord	Follow-up Phase Ongoing through 5 yrs.
NeoChord DS1000	NCT04190602	Multicenter Post-Market Observational Registry of the NeoChord Artificial Chordae Delivery System	AcChord	Recruiting

(a) TACT Registry

The TACT Registry is a Post-Market Surveillance Registry (NCT01784055, RP-610404-600 Version 1.0), which helped to develop the procedure and the training of physicians who use the device. This Post Market Surveillance study included more patients (126 versus 30) than the original CE Mark study (TACT Trial) and reflected some of the learnings from the original study. Of the 126 enrolled patients, 98% were implanted with at least one artificial chordae using the study device. After 58 subjects were enrolled (Initial cohort), procedural refinements were documented at each participating center and the learnings were applied to the remaining 68 subjects (post-notice cohort, documented in FSCA: FA-2014-001, issued on 27 March 2014) enrolled in the TACT Registry.

Investigators in the initial registry experience (initial cohort) identified 3 key observations which were included in this FSN:

- Importance of patient selection
- Location of access point in the left ventricle
- Relevance of preserving intact native chordae

All subjects in the post-notice cohort were implanted with two (2) or more chords. 93% of the patients in the initial cohort and 100% of the patients in the post-notice cohort left the OR with mitral regurgitation grade ≤2+. Procedure success was assessed prior to discharge and defined as the rate of subjects with at least one artificial chordae placed and with an accompanying reduction in mitral regurgitation of ≤ 2+, as evaluated by the Core Laboratory. In the initial cohort 81% and in the post-notice cohort 84% of patients had successful procedures.

Effectiveness was assessed as the durability of mitral regurgitation reduction from discharge to 12-months, as evaluated by the Echo Core Laboratory (ECL). Of the subjects who achieved procedural success after the index procedure, the results showed a significant improvement in the post-notice cohort compared to the initial cohort. 92% of the post-notice cohort maintained

mitral regurgitation ≤2+ at the 12-month visit and did not require mitral valve re-intervention. In the initial cohort, this concerned 65% of the patients.

The change as noted in the FSN resulted in an improvement in the rates of adverse events. Procedure related adverse events were reported in 38% of the patients in the initial cohort and in 22% of the patients in the post-notice cohort. Device related adverse events (MR - Implanted chord detachment or dehiscence (n=2), MR - leaflet restriction (n=1), MR - native chordae rupture (n=1), MR - unknown etiology (n=1), stroke (n=1)) were reported in 9% of the patients in the initial cohort and only 1% of the patients in the post-notice cohort.

When the data from the TACT Trial and TACT Registry was examined in aggregate, it was seen that as NeoChord continued to examine those factors that improved outcomes of the procedure and modified the procedure accordingly, the efficacy results continued to improve, and the procedure resulted in fewer device and procedure related adverse events. NeoChord will continue to examine criteria which lead to a more durable result.

In both TACT studies, patients who were not successfully treated with the device were able to undergo conventional mitral valve repair or replacement. The NeoChord procedure does not alter the natural anatomy of the mitral valve apparatus and preserves these other treatment options. The safety and performance data summarized in these reports support the continued market use of the NeoChord DS1000 System for the replacement of chordae tendinae.

(b) ReChord Study (US IDE)

A prospective, multicenter clinical investigation (NCT02803957) was initiated in November 2016 to gather data on the NeoChord DS1000 in support of the premarket approval application to the US FDA. The data from this clinical investigation is intended for publication in scientific journals, and to supplement post-market information for the NeoChord DS1000, when used as intended. Up to 615 subjects will be enrolled at up to 30 participating investigational sites including approximately 450 randomized subjects, up to 90 non-randomized, roll-in subjects, and up to 75 non-randomized, High Risk Registry subjects.

The annual progress report (PR-610405-107, Version 1.0, 16 May 2024) notes that currently 108 subjects have been enrolled at 15 sites, including 35 in the roll-in cohort, 69 in the randomized cohort, and 4 in the High-Risk Registry. Of these 108 enrolled patients, 71 underwent mitral valve repair using the study device, and 37 were randomized to the control group and underwent mitral valve repair using standard surgical techniques. Of the 108 enrolled subjects, 14 remain active in the study and 89 have completed the 1-Year follow-up visit. One hundred three (103) of the 108 attempted procedures (95%) were successfully completed as intended (67 Study Device and 36 Control group), with patients demonstrating a reduction in observed MR immediately following the procedure.

There were 543 adverse events reported in 101 out of 108 subjects. Of these 543 adverse events, 189 (35%) were serious adverse events (SAEs) reported in 77 subjects. There were no unanticipated adverse device effects. Of the SAEs, 39 were related to cardiac arrhythmias (14 in control group, all procedure-related; and 25 in roll-in/treatment/High-Risk group, 12 procedure- and device-related, 7 procedure-related only, and 5 not related to procedure/device). Eighteen

were related to cardiac-mitral, 28 were related to cardiac-other and 26 were related to cardiovascular-other. Fourteen (14) SAEs were non-specific, and 15 were related to pulmonary/respiratory. Nine SAEs concerned hepatic/renal issues, and in 17 cases the SAE was related to neurologic/nervous/psychiatric issues. Nine (9) SAEs were related to blood/lymphatic/endocrine, 6 were related to gastrointestinal/ genitourinary, 5 were related to muscular skeletal/dermatologic, and 3 were related to neoplasms (benign, malignant, and unspecified.

There were five (5) deaths reported, two (2) of which were unrelated to the procedure and study device, and one (1) death whereby the relation was unknown. This death concerned a cardiovascular event at 249 days after the procedure with an unknown cause. Two (2) more deaths are pending CEC adjudication, a cardiac event 1775 days after the procedure (treatment arm) and a stroke event 1785 days after the procedure in the control arm.

There were 13 re-interventions reported after successful completion of the index procedure. The primary cause of re-intervention included artificial chordae structural defect (3), chordal rupture (2), leaflet damage (2), leaflet prolapse/flail (1), chordal damage (1) and artificial chordae detachment (1). For the three (3) cases pending adjudication, the site-reported associated AE was recurrent MR.

To date, there were 18 cases of recurrent moderate (Grade 3+) or severe (Grade 4+) MR, in 12 cases, the patient underwent mitral valve re-interventions as treatment. The remaining patients continue to be monitored.

The study remains active and data collection and monitoring continues to occur, though no new patients are being enrolled currently.

(c) AcChord Registry

A PMCF registry (AcChord Registry) has been designed in line with ISO 14155:2020 guidelines to proactively collect and evaluate clinical data of the NeoChord DS1000 within its intended purpose. A synopsis of the PMCF registry design is outlined in **Table 6.**

At the time of this update, approximately 205 of the potential 500 patients have been enrolled in the AcChord Registry. While no formal analysis has been completed to date, summary data is provided.

All 205 patients had Grade III-IV MR at the time of treatment with the DS1000 device. Post-procedure, 98% had Grade 0-2 MR. There are 149 patients that have reached the 3-6 follow-up visit, with 87% reporting Grade 0-2 MR, and 88% at 1 year in the 129 patients providing follow-up. Similar improvements are seen the enrolled patient's NYHA classifications, with 50% of patients >Class III at enrollment, and just 5% and 8% being >Class II at the 6-and 12-month visits, respectively. No device related major adverse events or deaths have been reported in the registry.

TABLE 8 provides an overview of ongoing or planned post-market clinical follow-up

TABLE 8. POST-MARKET CLINICAL FOLLOW-UP

Aims	Description of the method/procedure	Objective to be addressed	Timelines
1. Confirming the safety and performance of the device throughout its expected lifetime. 2. Identifying previously unknown side-effects and monitoring the identified side-effects and contraindications. 3. Ensuring the continued acceptability of the benefit-risk ratio. 4. Identifying possible systematic misuse or off-label use of the device, with a view to verifying that the intended purpose is correct.	PMCF Registry	AcChord Registry: Obtain clinical data to further describe the treatment outcomes with the NeoChord DS1000, in a real-world population	Start: Q1 2020 Expected End date: Q4 2027
	PMCF Clinical Investigation	ReChord Study: Assess the safety and effectiveness of the study device in subjects with degenerative mitral valve disease receiving a mitral valve repair without cardiopulmonary bypass (treatment group) when compared to subjects receiving mitral valve repair using standard surgical techniques with cardiopulmonary bypass (control group).	Start: Q4 2016 Expected End date: Q3 2027
	Off-label use identification (part of PMS procedures)	Identify off-label use, if present.	Ongoing part of PMS activities; no start/stop dates.
	CER Literature Review	The clinical evaluations were performed to collect, appraise and analyze clinical data pertaining to the NeoChord DS1000, as manufactured by NeoChord Inc. and to evaluate whether there is sufficient clinical evidence to confirm that these products, when used according to their IFU, comply with the relevant Essential Requirements pertaining to the clinical performance and clinical safety as defined in Medical Device Regulations (MDR) 2017/745: Annex I. According to MEDDEV 2.7/1 Rev.4:2016, the relevant General Safety and Performance Requirements are considered GSPR 1, 5b, and 8.	The CER is a living document and is updated annually.

6. Possible Diagnostic or Therapeutic Alternatives

The table below **(TABLE 9)** provides an overview of potential alternative therapies to the NeoChord DS1000. Based on the available literature and clinical evidence evaluated as part of the clinical evaluation of the NeoChord DS1000, it appears that the device may be used to repair chordal elongation and rupture to reduce MR. Safety endpoints are comparable to rates reported for other percutaneous devices indicated for MR repair. The NeoChord DS1000 is the only currently available option that allows for replacement of elongated or ruptured native chordae while the heart remains beating.

TABLE 9. OVERVIEW OF ALTERNATIVE TREATMENTS

Device/Surgical option	Intended Purpose	Mode of Action
Open-heart surgery for Mitral Valve Repair		
Artificial Chordae	Replacement of the elongated or ruptured chordae.	Chordae is replaced with polytetrafluoroethylene sutures through the papillary muscle head.
Carpentier Resection	Repair the mitral valve, used in cases of posterior leaflet prolapse	Resection of the abnormal leaflet and the respective abnormal chordae. Stitch together the margin of the resected leaflet.
Annuloplasty	Rings or bands to restore the normal shape and circumference of the valve	Flexible or rigid rings, complete or incomplete rings, depending on annulus size and pathology.
Transcatheter Mitral Valve Repair		
MitraClip *PASCAL System* *Harpoon*	Repair mitral valve in a minimally invasive way.	Minimally invasive alternative to edge-to-edge surgical repair, by attaching the valve edges with a clip (MitraClip, PASCAL) or by sutures (Harpoon).
Open-heart Surgery for Mitral Valve Replacement		
Mechanical	Replace dysfunctional valve by a mechanical heart valve	Three main designs: caged ball valve, mono-leaflet valve, bi-leaflet valve
Bio-prostheses	Replace dysfunctional valve by a bioprosthetic heart valve	Bovine pericardium or porcine valve tissue treated with glutaraldehyde.
Transcatheter Mitral Valve Replacement		
Self-expanding nitinol frame with 3 bovine leaflets.	Replace mitral valve	Transcatheter valve implantation can be performed through transfemoral-transseptal or transapical approach.
Vasodilators, beta-blockers, spironolactone, nitrates, diuretics, sodium nitroprusside.	Not specifically to treat or cure mitral valve regurgitation.	Drugs in case surgery is not an option.

7. Suggested Profile and Training for Users

This device is intended to be used by physicians that have received training on the use of the device. Use of the device requires a minimum of one trained physician /operator and one trained member of the operating room staff. More specifically, as by SOP-18-2 (Rev E) (i.e., Physician Training and Qualification Plan), the curriculum and training requirements of physician use of the NeoChord DS1000 are defined. The coursework intends to teach terms and elements of the NeoChord DS1000 device and procedure. The training plan includes practical and experiential content which focuses on demonstrating device-use competency and procedural know-how. The plan includes simulation training, case observations, and

proctor-supported cases. As by SOP-18-3 (Rev E) (NeoChord Procedure Educators Training and Qualification Plan), educators are trained in order to train physicians, echocardiographers, and support staff on the NeoChord procedure. Moreover, the NeoChord Commercial Use and Clinical Case Support Plan (700251-001 Rev 6) provides the training requirements associated with the commercial use of the NeoChord DS1000 and defines the requirements for supporting clinical cases.

8. Reference to any Harmonized Standards and Common Specifications Applied

Standard	Year	Title
ASTM D4169	2022	Standard Practice for Verification & Validation of Shipping Containers and Systems
ASTM F1980	2016	Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices
BS EN ISO 20417	2021	Information supplied by the manufacturer – Medical Devices
BS EN ISO 10993-1	2020	Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process
BS EN ISO 11135	2014+A1:2019	Sterilization of health-care products - Ethylene oxide - Requirements for the development, validation and routine control of a sterilization process for medical devices
BS EN ISO 11607-1	2020+A1:2023	Packaging for terminally sterilized medical devices - Part 1: Requirements for materials, sterile barrier systems and packaging systems
BS EN ISO 11607-2	2020+A1:2023	Packaging for terminally sterilized medical devices - Part 2: Validation requirements for forming, sealing and assembly processes
BS EN ISO 11737-1	2018+A1:2021	Part 1: Determination of a Population of Microorganisms on Products, Sterilization Of
BS EN ISO 13485	2016+A11:2021	Medical Devices – Quality management systems-requirements for regulatory purposes
BS EN ISO 14155	2020	Clinical investigation of medical devices for human subjects - Good clinical practice
BS EN ISO 14971	2019+A11:2021	Medical Devices – Application of risk management to medical devices
IEC 60601-1	2012 (2005+A1:2012+A2:2020)	Medical electrical equipment - Part 1: General requirements for basic safety and essential performance
BS EN 60601-1:	2006+A2:2021	Medical electrical equipment - General requirements for basic safety and essential performance
IEC 60601-1-2	2014+A1:2020 Edition 4.1	Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance - Collateral Standard: Electromagnetic disturbances - Requirements and tests
BS EN 60601-1-2	2015+A1:2021	Medical electrical equipment - General requirements for basic safety and essential

Standard	Year	Title
		performance. Collateral Standard: Electromagnetic disturbances. Requirements and tests
BS EN 60601-2-18	2015	Medical electrical equipment - Particular requirements for the basic safety and essential performance of endoscopic equipment
BS EN 62471	2008	Photobiological Safety of Lamps and Lamp Systems
IEC 62366-1	2015+A1:2020	Medical Devices – Application of usability engineering to medical devices
BS EN 62366-1	2015+A1:2020	Medical Devices – Application of usability engineering to medical devices
IEC 62366-2	2016+A1:2020	Medical devices - Part 2: Guidance on the application of usability engineering to medical devices
BS EN ISO 14644-1	2015	Cleanrooms and associated controlled environments – Part 1: Classification of air cleanliness by particle concentration
BS EN ISO 14644-2	2015	Cleanrooms and associated controlled environments - Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration
BS EN ISO 14644-4	2022	Cleanrooms and associated controlled environments -- Part 4: Design, construction and start-up
BS 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
BS ISO 15223-2	2010	Medical devices – Symbols to be used with medical device labels, labelling, and information to be supplied – Part 2: Symbol development, selection and validation
BS EN ISO 22442-1	2020	Medical devices utilizing animal tissues and their derivatives – Part 1: Application of risk management
BS EN ISO 22442-2	2020	Medical devices utilizing animal tissues and their derivatives – Part 2: Controls on sourcing, collection and handling

9. Revision History

SSCP Revision	Date Issued	Change Description	Revision validated by the Notified Body
A	01-OCT-2024	Initial Notified Body Validated Version	☒ Yes Validation language: English ☐ No
B	05-Dec-2024 | 15:53 EST	2024 Annual updates to align with related plans and reports.	☒ Yes Validation language: English ☐ No

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