SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Aortic valve, prosthesis, percutaneously delivered
Device Trade Name:	Medtronic Evolut PRO+ system Medtronic Evolut FX system Medtronic Evolut FX+ system
Device Procode:	NPT
Applicant's Name and Address:	Medtronic, Inc. 710 Medtronic Parkway, Minneapolis, MN 55432
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P130021/S174
Date of FDA Notice of Approval:	08/28/2025

The original PMA for the Medtronic CoreValve system, P130021, was approved on January 17, 2014, with an indication for the treatment of symptomatic severe native calcific aortic stenosis in patients who are judged by a heart team to be at extreme risk for surgical aortic valve replacement (SAVR). Subsequently, the device was iterated and the indication was expanded via various PMA supplements, as summarized below:

- P130021/S002: Approved on June 12, 2014, for the CoreValve system to include patients with symptomatic severe native calcific aortic stenosis who are deemed to be at high risk for SAVR.
- P130021/S010: Approved on March 30, 2015, for the CoreValve system to include patients with a failing (stenosed, insufficient, or combined) surgical bioprosthetic aortic valve (transcatheter aortic valve-in-surgical aortic valve, or TAV-in-SAV) who are deemed to be at high or greater risk for redo SAVR.
- P130021/S033: Approved on July 10, 2017, for the CoreValve system, CoreValve Evolut R system, and CoreValve Evolut PRO system to include patients with symptomatic severe native calcific aortic stenosis who are deemed to be at intermediate risk for SAVR.
- P130021/S058: Approved on August 16, 2019, for CoreValve Evolut R system and CoreValve Evolut PRO system to include patients with symptomatic severe native calcific aortic stenosis who are deemed to be at low risk for SAVR.

The SSEDs to support the above indications are available on the following FDA websites and are incorporated by reference herein:

- https://www.accessdata.fda.gov/cdrh_docs/pdf13/P130021b.pdf
- https://www.accessdata.fda.gov/cdrh_docs/pdf13/P130021S002b.pdf
- https://www.accessdata.fda.gov/cdrh_docs/pdf13/P130021S010B.pdf
- https://www.accessdata.fda.gov/cdrh_docs/pdf13/p130021s033b.pdf
- https://www.accessdata.fda.gov/cdrh_docs/pdf13/P130021S058B.pdf

The current supplement expands the indication for use of the Evolut PRO+, Evolut FX and Evolut FX+ systems to include patients with a failing transcatheter bioprosthetic aortic valve (i.e., TAV-in-TAV or redo TAVR) who are deemed to be at high or greater risk for surgical therapy.

II. INDICATIONS FOR USE

The Medtronic Evolut PRO+, Evolut FX, and Evolut FX+ systems are indicated for use in patients with symptomatic heart disease due to failure (stenosed, insufficient, or combined) of a surgical or transcatheter bioprosthetic aortic valve who are judged by a heart team, including a cardiac surgeon, to be at high or greater risk for open surgical therapy (i.e., predicted risk of surgical mortality ≥8% at 30 days, based on the STS risk score and other clinical co-morbidities unmeasured by the STS risk calculator).

III. CONTRAINDICATIONS

The Medtronic Evolut PRO+, Evolut FX, and Evolut FX+ systems are contraindicated in patients who cannot tolerate Nitinol (a nickel titanium alloy), gold (specific to Evolut FX and Evolut FX+), an anticoagulation/antiplatelet regimen, or who have active bacterial endocarditis or other active infections.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the labeling for the Medtronic Evolut PRO+, Evolut FX, and Evolut FX+ systems.

V. DEVICE DESCRIPTION

The Medtronic Evolut PRO+, Evolut FX, and Evolut FX+ systems each consists of three components: the TAV, the Delivery Catheter System (DCS), and the Loading System (LS).

The Evolut PRO+ TAV (EVPROPLUS-23-US, EVPROPLUS-26-US, EVPROPLUS-29-US, EVPROPLUS-34-US), as shown in Figure 1, features a Nitinol frame that supports a trileaflet porcine pericardial tissue valve. The valve is sutured onto the frame using a polymer suture. Additionally, the valve features a porcine pericardial tissue external

frame wrap to minimize paravalvular regurgitation. The tissue undergoes treatment using Medtronic's alpha-amino oleic acid (AOA) process.

The Evolut FX TAV (EVOLUTFX-23, EVOLUTFX-26, EVOLUTFX-29, EVOLUTFX-34), as shown in Figure 1, is a design iteration of the Evolut PRO+ TAV. It retains all the features of the Evolut PRO+ TAV while adding radiopaque gold markers located at the target implant depth to enhance visualization during placement and thus improve procedural precision.

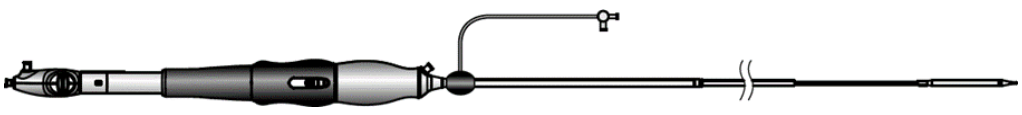
Figure 1: Evolut PRO+/FX Transcatheter Aortic Valve

The Evolut FX+ TAV (EVFXPLUS-23, EVFXPLUS- 26, EVFXPLUS-29, EVFXPLUS-34), as shown in Figure 2, builds on the Evolut FX TAV. It maintains the same features but introduces expanded windows behind each of the three valve leaflets for post implant access to the coronary ostia during potential future percutaneous coronary interventions.

Figure 2: Evolut FX+ Transcatheter Aortic Valve

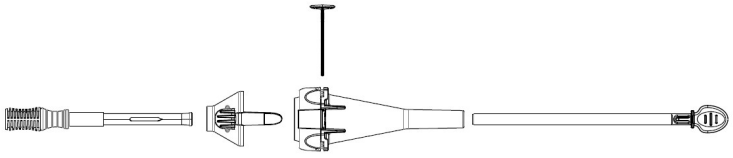
The Evolut PRO+ DCS (D-EVPROP2329-US, D-EVPROP34-US), as shown in Figure 3, used with the Evolut PRO+ TAV is an intravascular, over-the-wire delivery catheter which incorporates a protective deployment sheath that houses and deploys the bioprosthesis. The Evolut FX DCS (D-EVOLUTFX-2329, D-EVOLUTFX-34) represents an iterative design enhancement of the Evolut PRO+ delivery catheter system featuring modifications that reduce insertion and tracking forces while maintaining stability during deployment. It is also used to deploy the Evolut FX+ TAV.

Figure 3: Evolut Delivery Catheter System



The Evolut PRO+ Loading System (L-EVPROP2329-US, L- EVPROP34-US), as shown in Figure 4, is a system of reduction cones and tubing designed to gradually reduce the diameter of the TAV radially to an optimal diameter to facilitate manual loading into the deployment sheath capsule of the delivery system. The Evolut FX Loading System (L-EVOLUTFX-2329, L-EVOLUTFX- 34) is identical to the Evolut PRO+ loading system. It is also used to load the Evolut FX+ TAV.

Figure 4: Evolut Loading System



VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are other alternatives for patients with a failing transcatheter bioprosthetic aortic valve, including balloon aortic valvuloplasty (BAV) for temporary relief of stenosis, surgical replacement of the degenerated device, and palliative medical therapy without an obstruction-relieving procedure. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Medtronic Evolut PRO+ and Evolut FX systems are currently approved for the redo TAVR indication in 27 member states of the European Union (i.e., Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden), United Kingdom, and Turkey. The two systems have not been withdrawn from marketing for any reason related to their safety or effectiveness.

The Medtronic Evolut FX+ system has not been marketed in the United States or any foreign country for the redo TAVR indication.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of potential adverse effects (e.g., complications) associated with the use of the devices:

- Death
- Myocardial infarction, cardiac arrest, cardiogenic shock, cardiac tamponade
- Coronary occlusion, obstruction, or vessel spasm (including acute coronary closure)

- Cardiovascular injury (including rupture, perforation, tissue erosion, or dissection of vessels, ascending aorta trauma, ventricle, myocardium, or valvular structures that may require intervention)
- Emergent surgical or transcatheter intervention (e.g., coronary artery bypass, heart valve replacement, valve explant, percutaneous coronary intervention [PCI], balloon valvuloplasty)
- Prosthetic valve dysfunction (regurgitation or stenosis) due to fracture; bending (out-of-round configuration) of the valve frame; underexpansion of the valve frame; calcification; pannus; leaflet wear, tear, prolapse, or retraction; poor valve coaptation; suture breaks or disruption; leaks; mal-sizing (prosthesis-patient mismatch); malposition (either too high or too low)/malplacement
- Prosthetic valve migration/embolization
- Prosthetic valve endocarditis
- Prosthetic valve thrombosis
- DCS malfunction resulting in the need for additional re-crossing of the aortic valve and prolonged procedural time
- DCS component embolization
- Stroke (ischemic or hemorrhagic), transient ischemic attack (TIA), or other neurological deficits
- Individual organ insufficiency or failure (e.g., cardiac, respiratory, renal [including acute kidney failure]) or multi-organ failure
- Major or minor bleeding that may require transfusion or intervention (including life-threatening or disabling bleeding)
- Vascular access-related complications (e.g., dissection, perforation, pain, bleeding, hematoma, pseudoaneurysm, irreversible nerve injury, compartment syndrome, arteriovenous fistula, stenosis)
- Mitral valve regurgitation or injury
- Conduction system disturbances (e.g., atrioventricular node block, left-bundle branch block, asystole), which may require a permanent pacemaker implantation
- Infection (including septicemia)
- Hypotension or hypertension
- Hemolysis
- Peripheral ischemia
- Bowel ischemia
- Abnormal laboratory values (including electrolyte imbalance)
- Allergic reaction to antiplatelet agents, contrast medium, or anesthesia
- Exposure to radiation through fluoroscopy and angiography
- Permanent disability

For the specific adverse events that occurred in real-world clinical practice, please see Section X.

IX. SUMMARY OF NON-CLINICAL STUDIES

A summary of previously reported preclinical studies can be found in the SSED for the original PMA (https://www.accessdata.fda.gov/cdrh_docs/pdf13/P130021b.pdf).

Additional preclinical studies were performed on the Medtronic Evolut PRO+, Evolut FX, and Evolut FX+ systems in the redo TAVR configuration, as summarized in Table 1.

Table 1: Summary of Preclinical Studies for the Redo TAVR Configuration

Test	Test Description	Results
Effective orifice area	To verify the effective orifice area of the valve	Pass
Leaflet kinematics	To characterize the leaflet kinematics of the valve	For characterization only
Steady flow	To characterize the steady flow performance of the valve	For characterization only
Accelerated wear testing	To verify the valve durability to 200 million cycles	Pass
Dynamic failure mode	To characterize potential failure modes of the valve	For characterization only
Structural integrity	To verify the fatigue resistance of the valve frame through 600 million cycles	Pass
Migration resistance	To demonstrate that the valve can maintain position post implantation	Pass
Human factors engineering study	To validate that the whole system can support successful valve implantation	Pass

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed an analysis of the real-world off-label use data captured in the Society of Thoracic Surgeons (STS)/American College of Cardiology (ACC) Transcatheter Valve Therapy Registry (TVT-R) to establish a reasonable assurance of the safety and effectiveness of the Medtronic Evolut PRO+, FX, and FX+ systems (collectively referred to as Evolut systems, along with the earlier Medtronic Evolut R and PRO systems) in patients receiving redo TAVR treatment. The data from the TVT-R were the basis of the PMA approval decision. A summary of the clinical data is presented below.

Note that in addition to the Medtronic Evolut PRO+ and FX systems, the clinical dataset included the Medtronic Evolut R and PRO systems, which are no longer in commercial distribution, and did not include the Evolut FX+ system. Given the similarities among the various design iterations of the Evolut systems, the results obtained on the Evolut R and PRO systems are considered applicable to the later design iterations and the overall dataset is considered applicable to the Evolut FX+ system.

A. Study Design

A database extract was performed on February 7, 2025. To obtain complete 1-year follow-up data, a treatment cutoff date of September 30, 2023 was applied.

1. Clinical Inclusion and Exclusion Criteria

   The database extract included patients who received a commercially available Evolut valve for redo TAVR on or before the treatment cutoff date.

2. Follow-up Schedule

   All patients were followed post-implantation according to their local standards of care. The TVT-R collects follow-up data through 1 year.

3. Clinical Endpoints

   The TVR-R data were collected through standardized data collection forms. The endpoints analyzed in this application included rates of the following adverse events at 30 days and 1 year: all-cause mortality, stroke and TIA, aortic valve reintervention, valve performance based on echocardiographic data, New York Heart Association (NYHA) classification, and Kansas City Cardiomyopathy Questionnaire (KCCQ) score.

To augment the all-cause mortality outcome, linkage to Centers for Medicare and Medicaid Services (CMS) claims and encounter data was performed. In this analysis, mortality and follow-up data from CMS claims and encounter data were combined with the available data captured in the TVT-R to report all-cause mortality through 1 year (365 days). The linkage enabled additional mortality events and additional follow-up time to be included in the analysis for patients that were able to be matched.

B. Accountability of PMA Cohort

At the time of database extract, a total of 744 patients underwent a procedure, 740 of which had a valve implanted, which constitute the Attempted Implant (AI) population and Valve Implant (VI) population, respectively, as summarized in Table 2.

Table 2: Analysis Populations

	Number of Subjects
Attempted Implant Population	744
Valve Implant Population	740

A summary of the patient accountability at 30 days and 1 year in the TVT-R is shown in Table 3.

Table 3: Patient Visit Accountability in TVT-R (AI Population)

	Visit*	
	30 Day	**1 Year**
Total patients†	744	744
Ineligible	31	130
Death	26	98
Withdrawal	0	2
Lost to follow-up	5	30
Eligible‡	713	614
Follow-up visit completed	91.6% (653)	75.6% (464)
Missed visit	8.4% (60)	24.4% (150)

*30-day window: 23-75 days post procedure; 1-year window: 305-425 days post procedure.
†Total patients = # attempted implant
‡Number eligible = (total patients - # died - # withdrew - # lost to follow-up)

Of the 744 patients with an attempted implant captured in the TVT-R, 588 patients were able to be linked to the CMS claims and encounter data via a one-to-one match. Details on the matching information are shown in Table 4.

Table 4: TVT-R/CMS Data Matching Information

	TVT-R Records (N=744)	
	One-to-one Match	**No Match**
N	588	156
Medicare Fee-For-Service (%)	71.4%	N/A
Medicare Advantage (%)	28.6%	N/A

C. Study Population Demographics and Baseline Parameters

The patient demographics and baseline characteristics are summarized in Table 5, which reflect an elderly, multimorbid population, consistent with the high predicted operative risk of the population.

Table 5: Demographics and Baseline Characteristics (AI Population)

Demographics and Baseline Characteristics	Summary Statistics* (N=744)
Age (years)	78.9 ± 9.1 (744)
Male sex	39.9% (297/744)
Society of Thoracic Surgeons (STS) score	8.6 ± 7.6 (712)
New York Heart Association (NYHA) Class	
I/II	19.6% (144/734)
III/IV	80.4% (590/734)
Previous myocardial infarction	23.4% (174/744)
Previous intervention	
Coronary artery bypass grafting (CABG)	21.9% (163/744)
Percutaneous coronary intervention (PCI)	34.9% (260/744)
Aortic balloon valvuloplasty	9.3% (69/738)
Prior stroke or cerebrovascular accident (CVA)	13.8% (103/744)
Peripheral vascular disease (PVD)	24.3% (181/744)
Atrial fibrillation / Atrial Flutter	46.2% (344/744)
Permanent pacemaker or implantable cardioverter-defibrillator (ICD)	28.0% (208/744)
Porcelain aorta	3.0% (22/744)
Hostile chest	7.3% (54/744)
Echocardiographic findings (Valve Implant population)	
Aortic valve area (cm^2)	0.8 ± 0.3 (576)
Mean gradient across aortic valve (mmHg)	42.3 ± 16.5 (622)
Left ventricular ejection fraction (LVEF) (%)	52.5 ± 13.9 (732)
Moderate or severe aortic regurgitation	49.5% (365/737)
Moderate or severe mitral regurgitation	41.2% (263/638)

*Continuous measures - mean ± SD (total no.); categorical measures – % (no./total no.)

D. Safety and Effectiveness Results

1. Safety Results

The Kaplan-Meier estimates of adverse events through 1 year are summarized in Table 6. The Kaplan-Meier curve for all-cause mortality is presented in Figure 5, which shows a rate of 3.1% at 30 days and 16.2% at 1 year. The cardiovascular mortality rate was 2.1%

at 30 days and 5.4% at 1 year. The all-stroke rates were 3.7% and 4.3% at 30 days and 1 year, respectively.

Table 6: Site-Reported Adverse Events (AI Population)

Adverse Event	Kaplan-Meier Rate*	
	30 Days	1 Year
All-cause mortality†	3.1% (23, 23)	16.2% (114, 114)
Cardiovascular mortality	2.1% (15, 15)	5.4% (34, 34)
Any stroke	3.7% (27, 28)	4.3% (31, 32)
Ischemic stroke	3.5% (26, 26)	4.2% (30, 30)
Hemorrhagic stroke	0.3% (2, 2)	0.3% (2, 2)
Undetermined stroke	0.0% (0, 0)	0.0% (0, 0)
Transient ischemic attack	0.1% (1, 1)	0.9% (5, 5)
Major vascular complication	2.0% (15, 15)	2.2% (16, 16)
Life threatening/major bleeding	7.6% (56, 58)	9.0% (64, 69)
Myocardial infarction	0.3% (2, 2)	1.3% (8, 8)
New requirement for dialysis	1.2% (9, 9)	1.7% (12, 12)
Conduction/native pacer disturbance requiring pacer/implantable cardioverter-defibrillator (ICD)‡	5.0% (37, 37)	6.1% (43, 44)
Conduction/native pacer disturbance requiring pacer/ ICD§	6.8% (36, 36)	8.0% (41, 42)
Aortic valve re-intervention	0.7% (5, 5)	0.8% (6, 6)
Unplanned other cardiac surgery or intervention	1.5% (11, 11)	2.2% (15, 15)
Unplanned vascular surgery or intervention	5.1% (38, 42)	5.5% (40, 45)
Device thrombosis	0.1% (1, 1)	0.1% (1, 1)
Valve related readmission	0.3% (2, 2)	1.6% (10, 10)
Endocarditis	0.3% (2, 2)	0.7% (4, 4)

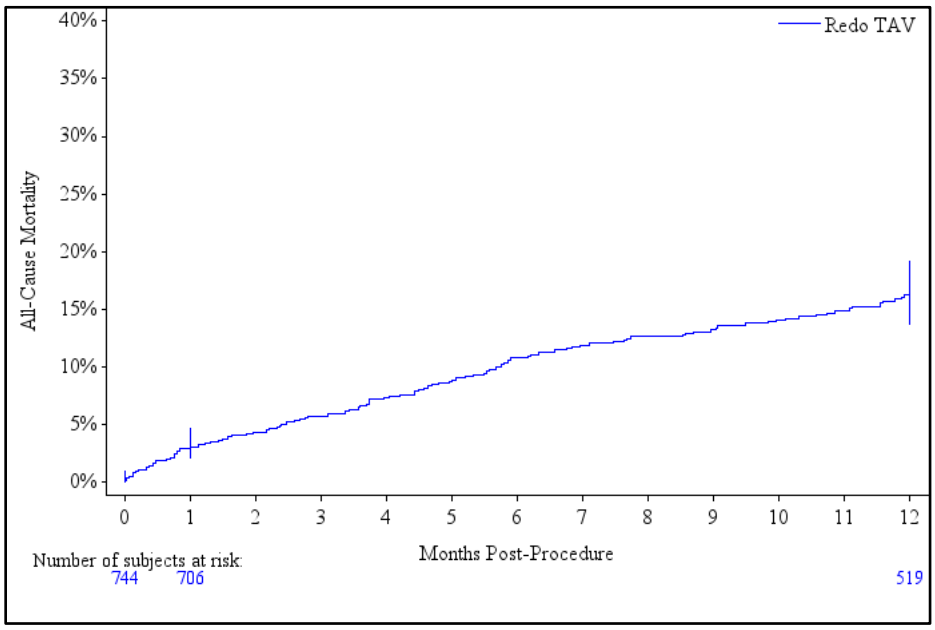
*Kaplan-Meier event rate (no. of patients with event, no. of events)

†All-cause mortality included both TVT-R data and CMS data.

‡Patients with pacemaker or ICD at baseline are included.

§Patients with pacemaker or ICD at baseline are not included.

Figure 5: All-Cause Mortality Through 1 Year (AI Population)



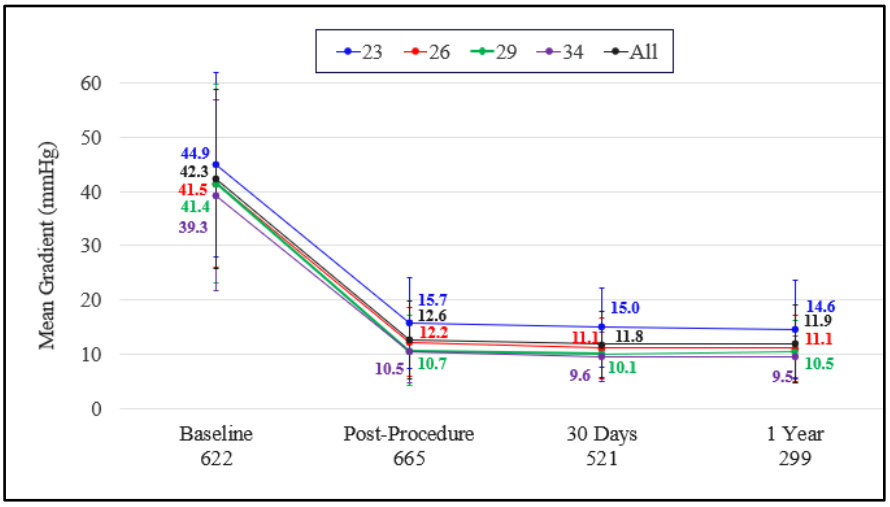
Note: The 95% confidence intervals were calculated without multiplicity adjustment. The adjusted confidence intervals could be wider than presented here. As such, confidence intervals are provided to illustrate the variability only and should not be used to draw any statistical conclusion.

2. Effectiveness Results

Valve Performance

The echocardiographic valve performance results are shown in Figure 6 through Figure 8. The mean aortic gradient decreased from 42.3 ± 16.5 mmHg at baseline to 11.8 ± 6.2 at 30 days, which was maintained through 1 year at 11.9 ± 7.1 mmHg. The percentage of patients had moderate or severe total aortic regurgitation was 49.6% at baseline, which decreased to 3.1% at 30 days and 3.0% at 1 year. The percentage of patients had moderate or severe paravalvular regurgitation was 2.3% at 30 days and 3.3% at 1 year.

Figure 6: Mean Aortic Gradient (VI Population)



Note: Line plot with mean and standard deviation. All patients with evaluable data at each time point.

Figure 7: Total Aortic Regurgitation Grade (VI Population)

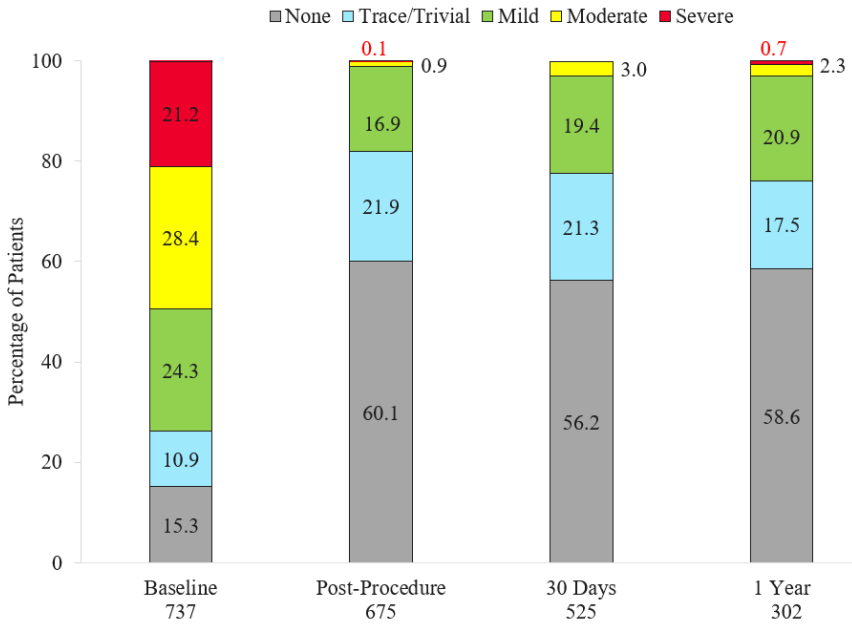
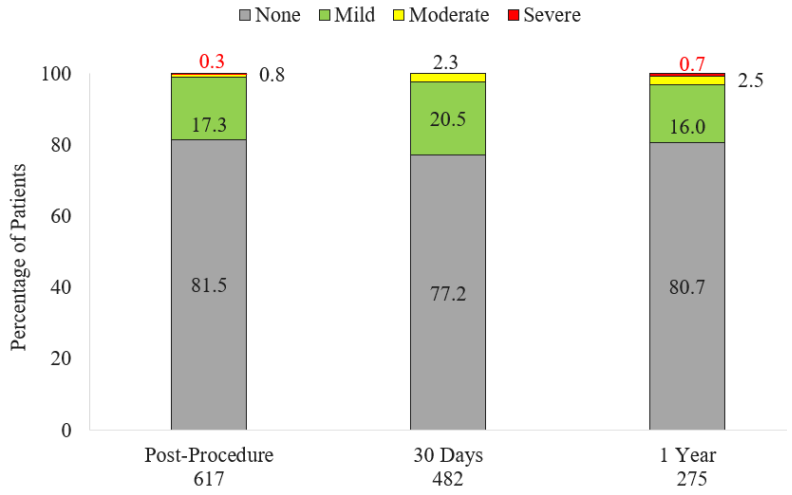


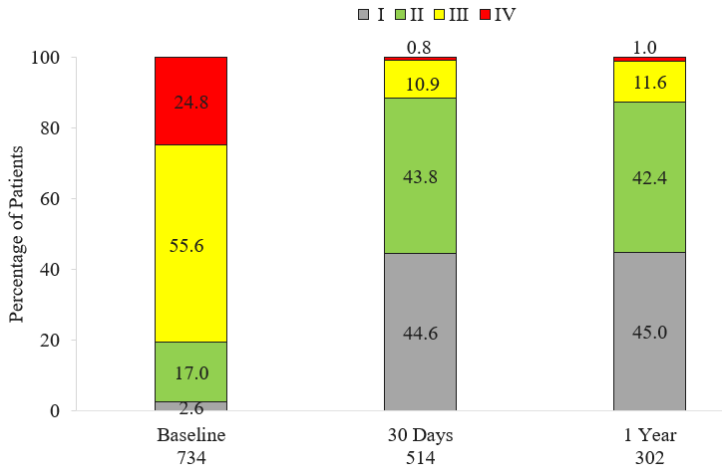
Figure 8: Paravalvular Regurgitation Grade (VI Population)



NYHA Functional Class

The NYHA functional class distributions by visit are presented in Figure 9. At baseline, 80.4% of patients were in NYHA class III/IV, which decreased to 11.6% at 30 days and 12.6% at 1 year.

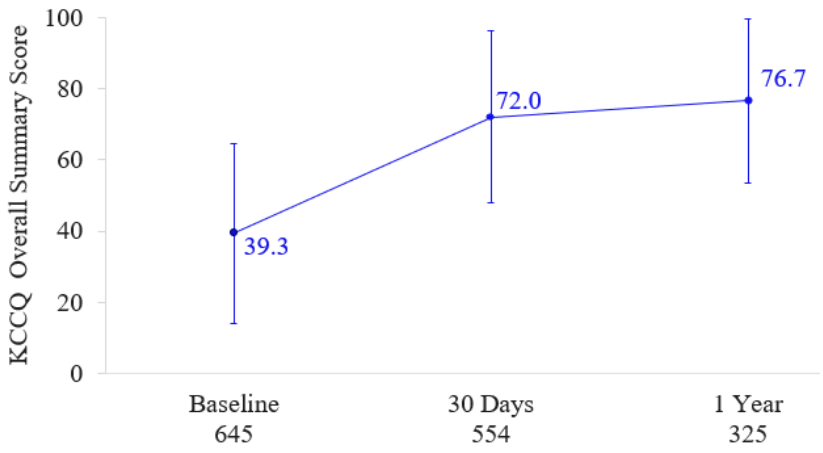
Figure 9: NYHA Class by Visit (AI Population)



KCCQ

The results for the KCCQ overall summary score are presented in Figure 10. The mean score improved from 39.3 at baseline to 72.0 and 76.7 at 30 days and 1 year, respectively.

Figure 10: KCCQ Overall Summary Score (AI Population)



Note: Line plot with mean and standard deviation. All patients with evaluable data at each time point.

3. Other Study Observations

Procedural Information

The procedural information is summarized in Table 7. The percentages of patients classified as inoperable/extreme risk and high risk for open surgery were 17.3% and 60.4%, respectively. The failed index transcatheter valve was an Evolut/CoreValve model in 9.3% of patients and unknown in the remaining 90.7% of patients. Successful device implantation was achieved in 99.3% of procedures with no reports of aborted procedures and three (0.4%) being converted to open heart surgery.

Table 7: Procedural Data Summary (AI Population)

Procedural Data	Summary Statistics* (N=744)
Operator reason for procedure	
Inoperable/extreme risk	17.3% (127/734)
High risk	60.4% (443/734)
Intermediate risk	19.2% (141/734)
Low risk	3.1% (23/734)
Failed index transcatheter valve model	
Evolut/CoreValve	9.3% (69/744)
Unknown	90.7% (675/744)
Implant approach	

Femoral & Iliac	94.5% (702/743)
Subclavian/axillary	3.0% (22/743)
Transcarotid	1.6% (12/743)
Direct aortic	0.5% (4/743)
Other	0.4% (3/743)
Implanted bioprosthesis model	
Evolut R	33.8% (250/740)
Evolut PRO	13.1% (97/740)
Evolut PRO+	31.8% (235/740)
Evolut FX	21.4% (158/740)
Valve size implanted (Valve Implant Population)	
23 mm	24.0% (177/739)
26 mm	46.3% (342/739)
29 mm	23.4% (173/739)
34 mm	6.4% (47/739)
Cardiopulmonary bypass used	0.4% (3/699)
Cardiopulmonary bypass status	
Emergent	66.7% (2/3)
Cardiopulmonary bypass time, minutes	115.0 ± 39.9 (3) 129.0 (70.0, 146.0)
Type of anesthesia	
General anesthesia	48.3% (359/744)
Deep sedation[†]	3.6% (27/744)
Moderate sedation	47.3% (352/744)
Minimal sedation[†]	0.7% (5/744)
Epidural[‡]	0.0% (0/744)
Combination[‡]	0.1% (1/744)
Total procedure time, minutes	94.9 ± 54.8 (744) 81.0 (62.0, 113.0)
Device implanted successfully	99.3% (738/743)
Procedure aborted	0.0% (0/744)
Conversion to open heart surgery	0.4% (3/744)
Conversion to open heart surgery reason	
Ventricular rupture	0.1% (1/744)

Annulus rupture	0.0% (0/744)
Other	0.3% (2/744)
Mechanical assist device in place at start of procedure	1.1% (8/744)

*Continuous measures - mean ± SD (Total no.), median (Q1, Q3); categorical measures – % (no./total no.)
†Only collected in procedures during or after 2021 (Version 3.0 TAVR Data Collection Form)
‡Only collected in procedures through 2020 (Version 2.1 TAVR Data Collection Form)

Length of Stay

The length of index hospitalization is summarized in Table 8. The median length of hospital stay was 2 days and the median length of stay in the intensive care unit was 1 day.

Table 8: Index Hospitalization (AI Population)

	Summary Statistics* (N=744)
Length of hospital stay after procedure (days)	3.9 ± 6.2 (744) 2.0 (1.0, 4.0)
Length of intensive care unit stay (days)†	2.0 ± 5.1 (362) 1.0 (0.0, 2.0)
Length of hospital stay after procedure ≤1 day	38.3% (285/744)

*Continuous measures - mean ± SD (total no.), median (Q1, Q3); categorical measures - % (no./total no.)
†Only collected for procedures through 2020 (Version 2.1 TAVR Data Collection Form)

4. Pediatric Extrapolation

In this premarket application, existing clinical data were not leveraged to support approval of a pediatric patient population.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the Act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The patients who underwent redo TAVR procedures captured in the TVT-R overall demonstrated clinically meaningful improvements in valve hemodynamics from baseline to

1 year. On average, the aortic valve pressure gradient decreased from 42.3 mmHg at baseline to 11.9 mmHg at 1 year. The proportion of patients with moderate or severe total aortic regurgitation decreased from 49.6% at baseline to 3.0% at 1 year.

The improvements in clinical outcomes were demonstrated in patients' functional status and health status. The majority (87.4%) of patients were in NYHA I/II at 1 year as compared to 19.6% at baseline. Similarly, clinically significant improvement was observed in the KCCQ overall summary score, which increased from 39.3 at baseline to 76.7 at 1 year on average.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory studies and clinical data collected in the TVT-R to support PMA approval as described above.

The Kaplan-Meier estimate of the all-cause mortality rate was 3.1% at 30 days (compared to a mean STS score of 8.6) and 16.2% at 1 year. The Kaplan-Meier estimates of all stroke, conduction/native pacer disturbance requiring pacer, and valve-related readmission were 4.3%, 8.0%, and 1.6%, respectively, at 1 year.

C. Benefit-Risk Determination

The probable benefits of redo TAVR with the Evolut systems include improved valve hemodynamic performance, improved functional status as measured by the NYHA classification, and improved health status as measured by the KCCQ.

The probable risks of redo TAVR with the Evolut systems include procedural and late complications such as death, stroke, and conduction/native pacer disturbance requiring pacer.

1. Patient Perspectives

   This submission did not include specific information on patient perspectives for this device. However, since transcatheter valve replacement with an Evolut system provides a less invasive alternative to surgical valve replacement, FDA believes many patients and their physicians would prefer the transcatheter valve replacement therapy as an alternative.

In conclusion, given the available information above, the data support that for patients with a failing (stenosed, insufficient, or combined) previously implanted transcatheter bioprosthetic aortic valve who are at high or greater risk for open surgical aortic valve replacement, the probable benefits of redo TAVR using an Evolut system outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of the Evolut systems in treating patients with symptomatic heart disease due to failing of

a transcatheter bioprosthetic aortic valve who are judged by a heart team, including a cardiac surgeon, to be at high or greater risk for open surgical therapy.

XIII. CDRH DECISION

CDRH issued an approval order on 08/28/2025. The final clinical conditions of approval cited in the approval order are described below.

The applicant must conduct one post-approval study:

Registry-Based Real-World Use Surveillance: The surveillance will be carried out to assess the real-world performance of the Evolut systems used for redo TAVR procedures. It will involve all consecutive patients treated within the first 2 years following device approval or a total of 500 consecutively treated such patients, whichever is greater, that are entered into the Society of Thoracic Surgeons (STS)/American College of Cardiology (ACC) Transcatheter Valve Therapy (TVT) Registry (enrollment period). All patients will be followed through 10 years post-procedure (follow-up duration). The clinical data through one (1) year will be collected through the TVT Registry. The follow-up data (including all-cause mortality, all stroke, and repeat procedure for valve-related dysfunction (surgical or interventional therapy) from year 2 through year 10 post-procedure will be obtained through linking the TVT Registry data with the Centers for Medicare and Medicaid Services (CMS) claims and encounter data.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.