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Tamara Syrek-Jensen, JD
Director, Coverage & Analysis Group
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

RE: Request for National Coverage Analysis for Tricuspid Valve Transcatheter Edge-to-Edge Repair (T-TEER)

Dear Ms. Syrek-Jensen:

Enclosed please find Abbott's formal request for a National Coverage Analysis (NCA) for tricuspid valve transcatheter edge-to-edge repair (T-TEER). Abbott believes that a national coverage policy for T-TEER will ensure long-term, predictable, and consistent coverage for all Medicare beneficiaries.

This request is driven by recently published scientific evidence showing that T-TEER is beneficial to patients with tricuspid valve regurgitation (TR) and parallel review of the TriClip™ therapy with the Food & Drug Administration (FDA).

The attached request provides key information for CMS to develop a National Coverage Determination (NCD) for T-TEER. We have also included some considerations for the NCD scope.

Thank you for your consideration of this request. If you have questions, please feel free to reach out to me or my colleagues with Abbott Health Economics & Reimbursement, Elizabeth Thoma (Elizabeth.Thoma@abbott.com) or Nicole Perzov (Nicole.Perzov@abbott.com).

Sincerely,

Barbara J. Calvert

Barbara J. Calvert

Optional URL

Request Contents

1. Formal Request

Abbott's TriClip™ therapy is participating in the Program for Parallel Review of Medical Devices (Parallel Review). The Premarket Approval application has been submitted to the FDA (PMA #P230007) and is under review by that agency and therefore we are submitting this formal request for a National Coverage Analysis (NCA) to evaluate tricuspid valve transcatheter edge-to-edge repair (T-TEER).

Currently, Abbott's TriClip™ therapy is available for commercial use in over 20 countries outside of the United States (e.g. Europe, Canada).

2. Benefit Category

Medicare beneficiaries would receive T-TEER under:

- Physician services (SSA Section 1861(q), (r), and (s)(1))
- Inpatient hospital services (SSA Section 1861(b))

3. Description of Service

3.1 Overview

The T-TEER procedure is intended to treat patients with symptomatic tricuspid regurgitation (TR). T-TEER procedures are performed percutaneously using a catheter-based technology to approximate the leaflets of the tricuspid valve with a clip device.

The T-TEER procedure using the TriClip™ device was developed leveraging the experience of the MitraClip™ therapy, which is used to treat mitral valve regurgitation using transcatheter edge-to-edge repair of the mitral valve.

3.2 Detailed Description of T-TEER

The patient is anesthetized, intubated, and imaging (e.g. transesophageal echocardiography (TEE), fluoroscopy) is performed for intraprocedural guidance.

The femoral vein is accessed and the site is predilated with step-up dilators and the steerable guide catheter is introduced into the femoral vein and advanced, sheath is placed into the right atrium using imaging guidance. While heparinized saline is flushed on the system's steerable guide catheter's hemostatic valve, alignment markers are used to correctly insert the tip of the implant delivery system into the steerable guide catheter valve and advanced. Using imaging guidance, the implant delivery system is advanced into the right atrium.

The implant is positioned over the desired line of coaptation of the tricuspid valve. Using imaging guidance, the implant position is verified in relation to the tricuspid valve leaflets. The implant is advanced, opened to grasp the leaflets, then closed, capturing the leaflets. In

order to confirm satisfactory clip positioning and leaflet insertion, three features are checked: 1) leaflet immobilization with creation of a single or multi-orifice valve; 2) limited leaflet mobility relative to the implant; and 3) decrease in TR. If needed, the implant can be opened, removed, and repositioned by releasing and regrasping the leaflets.

Leaflet coaptation and insertion is confirmed by allowing several minutes between shaft detachment and the final deployment step, monitoring the TR reduction and patient hemodynamics.

When satisfactory results are achieved, the implant is deployed. Following deployment of the initial implant, an additional implant(s) is positioned and deployed if TR reduction is not sufficient. Implants may be positioned along any line of leaflet coaptation.

The patient's arterial pressure, EKG waveforms, and oxygen saturation are constantly monitored throughout the procedure.

After completion of implants, the entire delivery system and the steerable guide catheter are removed. The groin site is closed per physician and institutional practices. Anesthesia is reversed and the patient is extubated as appropriate.

Hypertension, hypotension, bleeding and oxygen desaturation are common complications and are treated accordingly with medications and/or oxygen as needed during the procedure. The patient is transferred to the recovery suite for additional monitoring.

4. Scientific Evidence

In March 2023, results were published from the TRILUMINATE Pivotal randomized controlled trial, which studied the TriClip™ therapy in comparison to medical therapy. The primary endpoint of the trial was met demonstrating device superiority, driven mainly by significant improvement in quality of life.

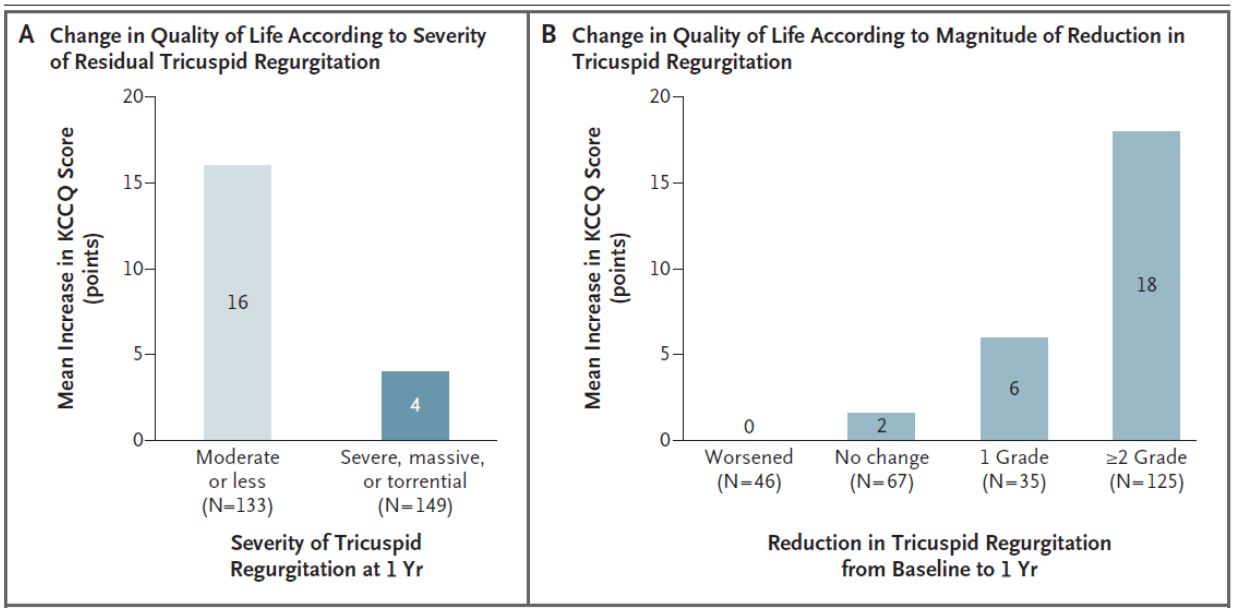
Table 1. TRILUMINATE Pivotal Summary and Results[1]

Trial Design	Prospective, randomized, controlled, multi-center trial designed to test the superiority of TriClip™ therapy in addition to medical therapy (Device group) over medical therapy alone (Control group) 450+ subjects enrolled at up to 80 sites in the US, Canada, Europe NCT 03904147	
Primary Endpoint	**To be assessed after the first 350 randomized subjects complete 12-month follow-up** A composite of mortality or tricuspid valve surgery, heart failure hospitalizations, and quality of life improvement ≥15 points assessed using the Kansas City Cardiomyopathy Questionnaire (KCCQ), evaluated at 12 months in a hierarchical fashion using the Finkelstein-Schoenfeld methodology	**Result: Met** Win ratio, 1.48 (1.06, 2.13), p=0.02
Secondary Endpoint	Assessed hierarchically in the following order:	**Results:**
	• Freedom from major adverse events (MAE) after procedure attempt (femoral vein puncture) at 30 days (Device group only)	**Met**, 98.3% p<0.001
	• Change in KCCQ at 12 months (superiority of Device vs. Control)	**Met**, 12.3pts vs. 0.6pts p<0.001
	• TR Reduction to moderate or less at 30-day post procedure (superiority of Device vs. Control)	**Met**, 87.0% vs. 4.8% p<0.001
	• Change in 6MWD at 12 months (superiority of Device vs. Control)	Not Met, -8.1m vs. -25.2m p=0.25

[1] Sorajja P, Whisenant B, Hamid N, Naik H, Makkar R, Tadros P, et al., Transcatheter Repair for Patients with Tricuspid Regurgiation. New England Journal of Medicine. 2023; Accessed Online March 4, 2023.

In addition, the degree of TR reduction was related to the degree of improvement in quality of life.

Figure 1. Changes in Quality of Life from Baseline to 1 Year, Stratified According to the Severity of Residual Tricuspid Regurgitation and the Magnitude of the Reduction in Tricuspid Regurgitation[2]



The randomized data available from TRILUMINATE Pivotal add to the existing evidence generated in the TRILUMINATE prospective single arm trial (**Table 2**) and the bRIGHT real-world study (**Table 3**).

[2] Figure 2. from Sorajja P, Whisenant B, Hamid N, Naik H, Makkar R, Tadros P, et al., Transcatheter Repair for Patients with Tricuspid Regurgiation. New England Journal of Medicine. 2023; Accessed Online March 4, 2023.

Table 2. TRILUMINATE Summary and Results[3]

Trial Design	Prospective single-arm multi-center trial designed to evaluate the TriClip™ therapy. 85 subjects enrolled at 21 sites in the US, Canada, Europe NCT 03227757	
Primary Endpoints	Safety: composite of major adverse events at 6 months, including cardiovascular mortality, myocardial infarction, stroke, new onset renal failure, endocarditis requiring surgery, and nonelective cardiovascular surgery for tricuspid valve repair system-related adverse events post procedure. Performance goal is 39%. Efficacy: reduction in TR severity by at least one grade at 30 days. Performance goal is 35%.	**Results:** Safety: **Met**, 4% Efficacy: **Met**, 86%

Table 3. bRIGHT Summary and Results[4,5]

Trial Design	Evaluate the real-world safety and effectiveness of TriClip™ in a prospective, single-arm, multi-center registry. Minimum 500 subjects at approximately 30 sites in Europe NCT 04483089	
Primary Endpoint	Acute Procedural Success defined as survival to discharge with successful implantation of the TriClip device with resulting TR reduction of at least 1 grade. Performance goal is 75%.	**Results:** **Met**, 91%
Secondary Endpoint	All-cause mortality or tricuspid valve re-intervention / re-operation at 1 year. Performance goal is 29%.	**Results:** **Met**, 17.6%

[3] Nickenig G, Weber M, Lurz P, von Bardeleben R, Sitges M, Sorajja P et al. Transcatheter Edge-to-Edge Repair for reduction of tricuspid regurgitation: 6-month outcomes of the TRILUMINATE single-arm study. Lancet. 2019 Nov 30;394(10213):2002-2011.
[4] Lurz P, Schmitz T, Bekeredjian R, Nickenig G, Moellmann H, von Bardeleben R, et al., editors. Real-world Outcomes for Tricuspid Edge-to-Edge Repair: Initial 1 Year Outcomes from the bRIGHT trial. PCR London Valves; 2022 27-29 November; London.
[5] Lurz P, Lapp H, Schueler R, Moellmann H, Nickenig G, et al. Real-world Outcomes for Tricuspid Edge-to-Edge Repair: Initial 30-Day Results from the TriClip™ bRIGHT Study. EuroPCR 2022 17-20 May; Paris, France.

The body of T-TEER evidence shows that TR reduction is effective and sustained. It also shows consistent, significant improvement in quality of life.

Table 4. Summary of TR Reduction and Quality of Life Improvement

Study	TR Moderate or Less		KCCQ-OS Improvement
	Baseline	1-year	1-year
TRILUMINATE[6,7]	6%	71%	20 points
bRIGHT[8]	2%	80%	21 points
TRILUMINATE Pivotal[9] (Device arm)	2%	89%	15 points*

**Note that for primary endpoint assessment, a KCCQ score of 0 was imputed for all patients who had a heart failure–related death from cardiovascular causes or received tricuspid-valve surgery before completing the 1-year follow-up. The investigators also reported the non-imputed improvement in KCCQ, which is included in this table.*

T-TEER provides clinical benefit in a very safe manner.

Table 5. Safety of TriClip™ Therapy

Study	Adverse Events (AE) through 30 Days					
	Cardiovascular mortality	New onset renal failure	Endocarditis requiring surgery	Non-elective cardiovascular surgery for TriClip device-related AE post-index procedure	Device thrombosis	Device embolization
TRILUMINATE[10]	0%	1.2%	0%	0%	0%	0%
bRIGHT[10,11]	0.3%	0.3%	0%	0.3%	0%	0%
TRILUMINATE Pivotal[9]	0.6%	1.2%	0%	0%	0%	0%

[6] Lurz P, Stephan von Bardeleben R, Weber M, Sitges M, Sorajja P, Hausleiter J, et al. Transcatheter Edge-to-Edge Repair for Treatment of Tricuspid Regurgitation. J Am Coll Cardiol. 2021;77(3):229-39.
[7] Von Bardeleben RS, Lurz P, Sitges M, Sorajja P, Hausleiter J, Ying SW, et al., editors. Percutaneous Edge-to-edge Repair for Tricuspid Regurgitation: 2-year Outcomes from the TRILUMINATE™ Trial. EuroPCR; 2021 18-20 May; Virtual Conference.
[8] Lurz P, Schmitz T, Bekeredjian R, Nickenig G, Moellmann H, von Bardeleben R, et al., editors. Real-world Outcomes for Tricuspid Edge-to-Edge Repair: Initial 1 Year Outcomes from the bRIGHT trial. PCR London Valves; 2022 27-29 November; London.
[9] Sorajja P, Whisenant B, Hamid N, Naik H, Makkar R, Tadros P, et al., Transcatheter Repair for Patients with Tricuspid Regurgiation. New England Journal of Medicine. 2023; Accessed Online March 4, 2023.
[10] Data on file at Abbott.
[11] Lurz P, Lapp H, Schueler R, Moellmann H, Nickenig G, et al. Real-world Outcomes for Tricuspid Edge-to-Edge Repair: Initial 30-Day Results from the TriClip™ bRIGHT Study. EuroPCR 2022 17-20 May; Paris, France.

5. Benefits and Relevance to the Medicare Population

Tricuspid valve disease is a progressive condition with poor prognosis. Current standards of care are unable to meet the rising challenge of treating 1.6M patients with moderate or greater TR in the United States[12,13]. Symptoms associated with TR, generally those of right-sided heart failure, include ascites, peripheral edema, hepatomegaly, decreased appetite, jugular vein enlargement and/or abdominal fullness.

Current treatment for tricuspid regurgitation involves medical therapy (focusing on improving TR symptoms[14]) or surgery, however surgery for isolated TR is rarely performed. Although ACC/AHA Guidelines list surgical intervention as a Class I recommendation if the patient has concomitant left-sided heart disease, it is not highly recommended to treat isolated TR due to high operative mortality risk[15].

Based on the age of study participants in the TRILUMINATE Pivotal, TRILUMINATE, and bRIGHT clinical trials, the demonstrated clinical benefits are relevant to the Medicare population.

Table 6. Patient Information for TriClip™ Trials

Study	Age, years	Male, %
TRILUMINATE[16]	77.8 ± 7.9	34
bRIGHT[17]	78.5 ± 7.6	47
TRILUMINATE Pivotal[18] (Device Arm)	78.5 ± 7.4	44
TRILUMINATE Pivotal (Control Arm)	77.8 ± 7.2	46

Compared with open surgery, transcatheter valve procedures often result in fewer complications and shorter lengths of stay, making them attractive options for Medicare beneficiaries. For TR patients who remain symptomatic despite stable medical therapy, a transcatheter option would be a benefit.

[12] Stuge et al. Emerging opportunities for cardiac surgeons within structural heart disease. J Thorac Cardiovasc Surg. 2006; 132 (6) p.1258-1261
[13] Leviner et al. Tricuspid Valve Replacement: The Effect of Gender on Operative Results. The Journal of Heart Valve Disease 2014; 23:209-215
[14] Rogers et al. The tricuspid valve. Circulation 2009; 119:2718-25
[15] Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol 2021; 77: 450-500.
[16] Nickenig G, Weber M, Lurz P, von Bardeleben RS, Sitges M, Sorajja P, et al. Transcatheter edge-to-edge repair for reduction of tricuspid regurgitation: 6-month outcomes of the TRILUMINATE single-arm study. Lancet. 2019;394(10213):2002-11.
[17] Lurz P, Schmitz T, Bekeredjian R, Nickenig G, Moellmann H, von Bardeleben R, et al., editors. Real-world Outcomes for Tricuspid Edge-to-Edge Repair: Initial 1 Year Outcomes from the bRIGHT trial. PCR London Valves; 2022; 27-29 November; London.
[18] Sorajja P, Whisenant B, Hamid N, Naik H, Makkar R, Tadros P, et al., Transcatheter Repair for Patients with Tricuspid Regurgitation. New England Journal of Medicine. 2023; Accessed Online March 4, 2023.

6. Future Considerations

There are already in existence two NCDs that address transcatheter valve therapies (NCD 20.32: Transcatheter Aortic Valve Replacement (TAVR) and NCD 20.33: Transcatheter Edge-to-Edge Repair (TEER) for Mitral Valve Regurgitation). In addition to commercially available therapies, there are numerous devices under clinical investigation for transcatheter treatment of valvular disease. While these therapies are still in development, decisions around the organization and scope of transcatheter valve policies should be considered in this context.

CMS could consider a therapy-focused NCD organization (e.g. NCD 20.33 amended to include TEER of both the mitral and tricuspid valves). As an existing example, NCD 20.7 covers Percutaneous Transluminal Angioplasty to "recanalize and dilate the vessel." It includes in its scope multiple anatomical locations including lower extremities, upper extremities, arteriovenous dialysis fistulas and grafts, and others.