*** Transmitted to Medical.Policy@Anthem.com***

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John Whitney, MD, **Vice President, Medical and Clinical Pharmacy Policy**
Evan London, MS, MPH, Director, Medical Policy
Office of Medical Policy and Technology Assessment (OMPTA)
Anthem Inc.

Re: Anthem's Transcatheter Valve Coverage Policy (SURG.0121)

Dear Dr. Whitney and Mr. London,

The Society for Cardiovascular Angiography and Interventions (SCAI) is a non-profit professional association with over 4,500 members representing interventional cardiologists. SCAI promotes excellence in interventional cardiovascular medicine through education, representation and the advancement of quality standards to enhance patient care.

Thank you for your detailed response to our recent letter on closure devices. We promise not to be writing you letters every couple of weeks! We do however see significant problems with your Transcatheter Valve Coverage Policy (SURG.0121). Anthem's aortic valve coverage policy is more restrictive than Medicare's and we see no reason for this. Additionally, Medicare already covers mitral valve procedures and is proposing to expand that coverage. We believe that Anthem's transcatheter valve policy is out of step with offering patients the best possible care for patients.

Transcatheter Aortic Valve Replacement (TAVR)

Anthem considers TAVR medically necessary only if the individual is at intermediate or greater risk for open surgical therapy. The PARTNER 3 trial which randomized 1000 patients with severe symptomatic aortic stenosis (AS) to TAVR using the SAPIEN 3 transcatheter heart valve (THV) or surgical aortic valve replacement (SAVR) showed lower rates of the composite outcome including death, stroke or 1-year hospitalization following TAVR compared to surgery.[1] Similarly, the Medtronic self-expanding THV was non-inferior to SAVR

among low-risk patients with severe symptomatic AS with respect to the composite end point of death or disabling stroke at 24 months.[2]

Based on the above studies, in August 2019, the Food and Drug Administration (FDA) granted approval for the Edward SAPIEN 3 and Medtronic's CoreValve Evolut THV systems in severe symptomatic AS patients at low operative risk for standard SAVR. The Centers for Medicare & Medicaid Services (CMS), in a national coverage determination decision memo determines that TAVR is covered for the treatment of symptomatic aortic valve stenosis when furnished according to an FDA-approved indication.[3] Under this decision, patients at low operative risk for standard SAVR have been covered.

In spite of this, Anthem still considers TAVR in severe symptomatic AS patients at low-risk for surgery to be "not medically necessary". Anthem requires long-term studies to establish the durability of TAVR in the low-risk population.

Bench testing demonstrates that the balloon expandable Sapien 3 THVs have excellent durability after accelerated wear testing to 1 billion cycles (an equivalent of 25-years) compared to the Magna Ease surgical valves.[4] At 2-years follow-up, the SAPIEN 3 THV is associated with similar trans-prosthetic gradients, valve area and percentage with severe patient-prosthesis mismatch or moderate/severe aortic regurgitation, compared to surgical valves.[5]

Based on clinical trial evidence, regulatory body decisions and available evidence regarding THV durability, Anthem's designation that TAVR "not medically necessary" among patients at low-risk for surgery restricts access to proven therapies among those with appropriate indications.

Transcatheter Mitral Valve Repair (TMVR) using the MitraClip Delivery System

Anthem considers Transcatheter mitral valve repair using leaflet repair (for example, MitraClip Clip Delivery System) investigational and not medically necessary for all indications.

TMVR using the MitraClip delivery system has received FDA approval when standard of care is not an option (prohibitive surgical risk for degenerative severe mitral regurgitation, MR) or ineffective (symptomatic despite guideline directed medical therapy in functional severe MR). Clinical trial evidence and post-marketing surveillance evidence demonstrate safety and efficacy when MitraClip is used for patients with degenerative MR at prohibitive risk for surgery and patients with functional MR that are symptomatic despite optimized medical therapy.

1. Approval from Regulatory Bodies

The MitraClip Clip Delivery System received FDA approval on October 24, 2014. The FDA labeling for the MitraClip Clip Delivery System supported the following indications for use: The MitraClip Clip Delivery System is indicated for the percutaneous reduction of significant symptomatic mitral regurgitation (MR ≥ 3+) due to primary abnormality of the mitral apparatus [degenerative MR] in patients who have been determined to be at prohibitive risk for mitral valve surgery by a heart team, which includes a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, and in whom existing comorbidities would not preclude the expected benefit from reduction of the mitral regurgitation.[6]

The FDA found the MitraClip Clip Delivery System for the treatment of regurgitation to "address an unmet clinical need in that it represents a breakthrough technology that provides a clinically meaningful advantage over existing technology by being the first available percutaneous mitral valve repair device".

The MitraClip Clip Delivery System, on March 14, 2019, received additional FDA approval for expanded indication for the treatment of secondary/functional mitral regurgitation in select individuals with heart failure who remain symptomatic despite guideline-directed medical therapy.

2. Credible Scientific Evidence

As described above, currently there are 2 FDA indications for transcatheter mitral valve repair using the MitraClip delivery system. Among patients with severe degenerative mitral valve regurgitation, it's indicated for patients who are not candidates for the standard of care which is surgical mitral valve repair or replacement and thus without other effective treatment options.

In the Everest II trial, in whom patients with grade 3+ or 4+ mitral regurgitation were randomly assigned to MitraClip or conventional surgery, at 5 years, mortality was higher in the surgery group 27% compared to 21% in the MitraClip group (not statistically significant, p-value 0.4).[7] The risk of mitral valve surgery or reoperation was higher in the MitraClip group (28% compared to 9% in surgery). Residual 3+ or 4+ MR was more prevalent in the MitraClip group (12% compared to 2% in surgery). In long-term follow-up MitraClip therapy was able to demonstrate similar mortality, stable mitral regurgitation reduction, albeit at a lower rate than seen for what remains the standard of care, surgery. The FDA thus approved the MitraCliip system to treat patients with severe degenerative mitral regurgitation who were at **prohibitive risk** for surgery and thus without other treatment options.

Surgical mitral valve repair or replacement has not been effective at improving long term outcomes in severe functional mitral regurgitation.[8] In a randomized controlled trial enrolling

301 patients, comparing the efficacy of mitral valve repair with CABG versus CABG alone among patients with moderate ischemic mitral regurgitation, there was no improvement in mortality, hospital readmission rates or LV remodeling. Thus, the standard of care for the treatment of severe functional mitral regurgitation remains **guideline directed medical therapy**. Two large randomized controlled trials explored TMVR using the MitraClip system in patients with severe functional mitral regurgitation. In the COAPT trial, 614 patients with functional severe mitral regurgitation, symptomatic despite medical therapy were randomized to medical therapy versus MitraClip therapy. Transcatheter mitral valve repair with MitraClip was associated with reduced heart failure hospitalization (36% in the device group compared to 68% in the medical therapy group).[9] Ninety-seven percent of patients in the device group were free of any complications. Death from any cause was lower in the device group (29% compared to 46% in the medical therapy group). In the MITRA-FR trial, 304 patients with severe functional mitral regurgitation were randomized to MitraClip or medical therapy. At 12 months, there was no difference in mortality or unplanned hospitalization.[10] One important difference between COAPT and MITRA-FR is the rigorous application of optimization of guideline-directed medical therapy under the direction of a HF specialist in thus COAPT trial. Thus, as shown in the COAPT trial when added to rigorous application of standard of care (guideline directed medical therapy), TMVR using the MitraClip system in severe symptomatic MR improved long-term outcomes including mortality and heart failure hospitalization.

3. Improvement Outside Investigational Setting

Since FDA approval post-marketing surveillance data on US MitraClip implants has been collected in the national Society of Thoracic Surgery/American College of Cardiology Transcatheter Valve Therapy (STS/ACC TVT) Registry. In 2017, Sorajja et al reported outcomes following MitraClip implant showing acute effectiveness and safety with the use of the technology. [11] Between November 2013 and September 2017, 2952 patients underwent transcatheter mitral valve repair using the MitraClip system in the United States. While the majority of patients treated in the US had degenerative MR, 9% had functional MR and another 9% had mixed (functional and degenerative) MR. In-hospital mortality was 2.7%, Stroke was seen in 0.4%. Single leaflet device detachment was noted in 1.5%. Acute procedural success was 92%. 1-year mortality was 26% and 1-year hospitalization was noted in 20%. At 1-year mitral valve surgery rate was 2.1% and repeat MitraClip intervention rate was 6.2%.

Anthem's designation of TMVR using the MitraClip Clip Delivery system as investigational and not medically necessary is not supported by evidence, regulatory body decisions and post-marketing surveillance studies. TMVR using the MitraClip delivery system has received FDA approval when standard of care is not an option (prohibitive surgical risk for degenerative severe mitral regurgitation) or ineffective (symptomatic despite guideline directed medical therapy in functional severe mitral regurgitation). TMVR has been covered by CMS for the treatment of symptomatic degenerative MR when furnished according to FDA approved

indications since August 2014.[12] CMS has also recently proposed expansion of the previous TMVR (now called trans-catheter edge-to-edge repair, TEER) coverage decision to include patients with symptomatic moderate-to-severe or severe functional MR despite guideline-directed medical therapy.[13]

We thank Drs. Kalkidan Bishu, James Hermiller and Steven Yakubov for their efforts in developing this communication. If you would like to communicate with SCAI about this policy, please contact Wayne Powell at wpowell@scai.org or 703.772.7910.

Sincerely

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