Clinical Policy Title: Total artificial heart

Clinical Policy Number: CCP.1250

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ABOUT THIS POLICY: AmeriHealth Caritas has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas’ clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by AmeriHealth Caritas when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas’ clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas’ clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas will update its clinical policies as necessary. AmeriHealth Caritas’ clinical policies are not guarantees of payment.

Coverage policy

The total artificial heart is clinically proven and, therefore, medically necessary as a bridge to transplantation when implantation is performed at a Medicare-approved heart transplantation facility or at a facility with a United Network for Organ Sharing-approved heart transplantation program for members who meet all of the following criteria (Feldman 2013; Peura, 2012; Ponikowski, 2016):

- Biventricular failure.
- Not expected to survive until a donor heart can be obtained.
- No other surgical or medical treatment options.
- Ineligible for univentricular or biventricular support devices.
- Candidate for heart transplantation or is undergoing evaluation to determine candidacy for heart transplantation.
- Receiving maximal medical therapy including intravenous inotropic support.

For Medicare members only:

The total artificial heart is medically necessary when use in accordance with National Coverage Determination 20.9 Artificial hearts and related devices.

Limitations:

Policy contains:
- Heart failure.
- Mechanical circulatory support.
- Total artificial heart.
All other uses of the total artificial heart are not medically necessary.

Absolute contraindications to the total artificial heart include conditions that would generally exclude patients for heart transplantation, including, but not limited to (Peura, 2012; Rihal, 2015; Yancy, 2013):

- Chronic irreversible hepatic or respiratory failure.
- Irreversible kidney failure unless bridge to heart–kidney transplantation is considered.
- Active systemic infection or prolonged intubation.
- Coagulation disorders.
- Irreversible kidney failure unless bridge to heart–kidney transplantation is considered.
- Insufficient space in the thorax and/or abdominal cavity for the device (e.g., body surface area < 1.7 m², or distance between the sternum and 10th anterior vertebral body measured by computed tomography < 10 cm).
- Structural heart disease that prohibits or may interfere with a successful implantation (e.g., uncorrected valvular disease).
- Underlying coagulopathy, either an international normalized ratio < 2.5 or a platelet count < 50,000. A contraindication to anticoagulation is a contraindication to mechanical circulatory support in most situations.

Relative contraindications include, but are not limited to (Peura, 2012; Ponikowski, 2016):

- Age > 80 years for destination therapy.
- Obesity > 40 kg/m² or malnutrition.
- Musculoskeletal disease that impairs rehabilitation.
- Untreated malignancy.
- Severe peripheral vascular disease.
- Active substance abuse.
- Impaired cognitive function.
- Unmanaged psychiatric disorder.
- Inadequate psychosocial support.

Alternative covered services:

- Cardiac rehabilitation.
- Cardiac resynchronization (implantable cardioverter-defibrillator; cardiac resynchronization therapy).
- Continuous intravenous inotropic infusion.
- Corrective surgery (e.g., coronary artery bypass or valve replacement).
- Extracorporeal membrane oxygenation.
- Heart transplantation.
- Intra-aortic balloon pump.
- Percutaneous coronary intervention.
Pharmacologic therapy, including but not limited to: Angiotensin-Converting Enzyme Inhibitors; Angiotensin II Receptor Blockers (or Inhibitors); Angiotensin-Receptor Neprilysin Inhibitors; \( \text{I}\) Channel Blocker (or inhibitor); Beta Blockers; Aldosterone Antagonists; Hydralazine and isosorbide dinitrate (specifically benefits African Americans with heart failure); diuretics; digoxin; statins; and anticoagulants.

**Background**

Heart failure is a complex clinical syndrome resulting from any structural or functional impairment of ventricular filling or ejection of blood that fails to meet the body’s needs (Yancy, 2013). Disorders of the pericardium, myocardium, endocardium, heart valves, great vessels, or certain metabolic abnormalities can cause heart failure and lead to episodes of arrhythmia, increasing pump failure, and premature death. Dyspnea and fatigue are the principal symptoms of heart failure; infants may also present with poor feeding, poor growth, excessive sweating, or even low blood pressure.

The class and type of heart failure are important considerations for managing patients with heart failure (American Heart Association, 2017). Most patients with heart failure have symptoms due to left ventricular impairment. Several validated classification systems are available to grade the severity of heart failure, including: the four-stage New York Heart Association functional classification; the American College of Cardiology/American Heart Association staging system; the European Society of Cardiology (European Society of Cardiology) system; and the Ross Classification System for infants and younger children (Rosenthal, 2004). The Interagency Registry for Mechanically Assisted Circulatory Support (2018), which acquires data on patients supported with U.S. Food and Drug Administration-approved mechanical circulatory support devices, further stratifies patients with advanced heart failure into seven clinical profiles by their signs and symptoms (See Appendix).

A subset of patients with chronic heart failure will continue to progress and develop persistently severe symptoms despite maximum guideline-directed medical therapy. Patients with advanced heart failure typically have symptoms at rest or with minimal exertion and cannot perform many activities of daily living. They are usually classified as American College of Cardiology/American Heart Association stage D or New York Heart Association Class IV and have clinically significant circulatory compromise (see Appendix).

**Mechanical circulatory support:**

Advanced heart failure is a debilitating condition for which heart transplantation offers the best treatment option. However, the supply of donor hearts is diminishing, and demand greatly exceeds supply. The shortage of donor hearts has encouraged the development of artificial mechanical devices that can assist or replace the function of the failing heart. A ventricular assist device is an electromechanical pump attached to the native heart and vessels to augment cardiac output. It is designed to partially or completely assist the ventricles of the native heart. A total artificial heart is attached to the pulmonary artery and aorta; it is designed to completely replace cardiac function and generally requires the removal of the patient's heart.
Surgically-placed ventricular assist devices are categorized by the implant location (implanted in the thorax or abdomen versus extracorporeal), flow characteristic (pulsatile versus continuous), pump mechanism (volume displacement, axial, or centrifugal), and the ventricle(s) supported (left, right, or biventricular). Percutaneous ventricular assist devices differ from other types of ventricular assist devices by using cardiac catheterization for placement, rather than open chest surgery, and a trans-septal approach to the left ventricle, which avoids potential difficulties in crossing the aortic valve.

The U.S. Food and Drug Administration (2019a, 2019b, 2019c) has approved several ventricular assist devices/total artificial heart for specific clinical uses in adult and pediatric populations. Ventricular assist devices may be necessary for short-term (days to weeks), intermediate-term, or long-term (months to years) use. Ventricular assist devices for short-term use are inserted surgically or percutaneously to facilitate cardiac catheterization procedures as a bridge to recovery. Devices for intermediate and long-term use are surgically implanted as intracorporeal devices or as extracorporeal devices as bridge to transplantation or destination therapy.

**Searches**

We searched PubMed and the databases of:
- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality.
- The Centers for Medicare & Medicaid Services.
- The Cochrane Library.

We conducted searches on July 19, 2019. Search terms were: “Heart-assist devices” (MeSH), “Heart, artificial” (MeSH), and free text terms “ventricular assist device” and “total artificial heart.”

We included:
- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews**.
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

We identified six systematic reviews or other evidence syntheses (Borisenko, 2014; Cheng, 2009; Health Quality Ontario, 2016; Lang, 2014; Neyt, 2016; Sutcliffe, 2013), six professional guidelines (Feldman, 2013; Peura, 2012; Ponikowski, 2016; Rihal, 2015; Rosenthal, 2004; Yancy, 2013), and three cost-effectiveness analyses (Maini, 2014; Long, 2014; Sutcliffe, 2013) for this policy. The evidence consists of predominately
retrospective case series and registry analyses. The highest quality evidence from randomized controlled trials and a majority of lower observational studies evaluated surgically-implanted left ventricular assist devices in adult populations (age 16 or older). The randomized controlled trials compared left ventricular assist devices to guideline-directed medical management as destination therapy, and percutaneous left ventricular assist devices versus intra-aortic balloon pumps for cardiogenic shock.

Ventricular assist devices are indicated for persons with end-stage heart failure with reduced ejection fraction (American College of Cardiology/American Heart Association stage D or New York Heart Association Class IV) who continue to progress and develop persistently severe symptoms despite maximum guideline-directed medical and device management. Most implanted ventricular assist devices were performed in persons classified at Interagency Registry for Mechanically Assisted Circulatory levels 1–3.

The primary goal of mechanical circulatory support, including ventricular assist devices, as a treatment strategy for patients presenting with advanced heart failure or cardiogenic shock is stabilizing a critically ill patient before making a decision regarding durable therapy. Newer generation implantable ventricular assist devices are smaller and more durable allowing for their use in myocardial recovery, possibly obviating the need for destination therapy. However, the distinction between the use of left ventricular assist devices as bridge to candidacy, when the therapeutic goal is to improve end-organ function in order to make an ineligible patient eligible for heart transplantation, bridge to transplantation, and destination therapy becomes somewhat arbitrary, as an increasing number of ventricular assist devices as bridge to candidacy will convert to destination therapy due to the limited number of heart donors (Neyt, 2016).

The evidence suggests ventricular assist devices may facilitate myocardial recovery for individuals with reversible ventricular dysfunction, temporarily maintain circulation until transplant, or extend the life expectancy of the terminally ill. They can improve survival, quality of life, and functional status but are accompanied by a range of common complications, particularly with the newer continuous-flow left ventricular assist devices. The most common adverse events are bleeding, thromboembolism, infection, right ventricular failure requiring inotropic support, renal failure, and device failure. Late bleeding occurs mainly from gastro-intestinal origin.

The cost-effectiveness of left ventricular assist devices will depend on many factors including the clinical indication, availability of donor hearts for transplantation, device used, and patient and provider preferences (Long, 2014; Maini, 2014; Sutcliffe, 2013). While ventricular assist devices may improve survival in many cases, associated adverse events and small improvements in quality of life may limit their cost-effectiveness below conventionally held willingness-to-pay thresholds. Limited randomized controlled trials and other comparative studies make reliance on registry data and other database information critical to gauging long-term cost-effectiveness.

Few randomized comparative studies are available to guide patient or device selection for the patient requiring mechanical circulatory support beyond criteria established for U.S. Food and Drug Administration approval. In adult populations, some generalizations from consensus-based guidelines can be made:
• As bridge to transplantation, the efficacy of surgically-implanted left ventricular assist devices is demonstrated in numerous uncontrolled trials and trials comparing different ventricular assist devices among patients awaiting heart transplantation who have no other options for survival. Evidence for earlier ventricular assist device implantation in less severely ill patients (e.g., those not yet on inotropic support) requires further study (Peura, 2012; Ponikowski, 2016; Yancy, 2013).

• As bridge to transplantation, biventricular assist devices and total artificial hearts are available for patients with biventricular heart failure who meet criteria for heart transplantation and are at risk of imminent death. The effectiveness of temporary total artificial heart has been established only in patients with idiopathic and ischemic cardiomyopathies in a hospital setting (Ponikowski, 2016).

• As destination therapy, ventricular assist devices improve outcomes in patients who are not candidates for heart transplantation and can be considered for patients who are expected to be on a long-term waiting list for heart transplantation (Borisenko, 2014; Health Quality Ontario, 2016; Peura, 2012; Sutcliffe, 2013). Patient selection is based on enrollment criteria in pivotal randomized controlled trials used to support U.S. Food and Drug Administration approval. Studies have not validated other preoperative variables to further refine patient selection and thereby improve patient outcomes. The safety and efficacy of biventricular assist devices or total artificial heart as destination therapy or total artificial heart used with a portable driver outside the hospital setting have not been established.

• The concept of bridge to candidacy has not been standardized, and the decision to label a given ventricular assist device implantation as bridge to candidacy (instead of either bridge to transplantation or destination therapy) may depend on several circumstances, such as the hemodynamic and general condition of the patient or donor availability (Neyt, 2016). Observational data suggest the overall, long-term survival with left ventricular assist devices as bridge to candidacy is in-between that of bridge to transplantation and destination therapy, but results from randomized controlled trials are lacking.

• As a bridge to recovery, ventricular assist devices approved for temporary use (extracorporeal or percutaneous ventricular assist devices) in specific situations are available, but evidence of effectiveness is limited and conflicting. Guidelines vary in their enthusiasm for percutaneous ventricular assist devices, but most recommend them as an option in the settings of percutaneous coronary intervention and cardiogenic shock/heart failure post-cardiotomy in patients for whom established treatments provide or are likely to provide inadequate hemodynamic support (Peura, 2012; Ponikowski, 2016; Rihal, 2015; Yancy, 2013). Extracorporeal ventricular assist devices provide temporary hemodynamic support for patients in acute heart failure or cardiogenic shock who otherwise faced an extremely high risk of mortality, but substantial uncertainty exists regarding the relative benefits versus alternatives (e.g., extracorporeal membrane oxygenation).
Ventricular assist devices have played an increasingly important role in the management of advanced heart failure in children (age 5 to 16 years) (Borisenko, 2014; Kirk, 2014). The predominant role of these devices has been as a bridge to transplantation with a demonstrated survival benefit based on multiple uncontrolled studies. Primary indications for mechanical circulatory support in pediatrics include heart failure related to congenital heart disease, cardiomyopathy and myocarditis, and cardiac allograft failure.

The most commonly used method of mechanical circulatory support in children is extracorporeal membrane oxygenation, and the only percutaneous device approved in the United States for short-term cardiac support in children is the intra-aortic balloon pump (Kirk, 2014). Extracorporeal membrane oxygenation is able to provide complete circulatory support in a wide range of patients from newborns to adults both with and without congenital heart disease, but it is highly invasive and survival rates remain low at 40 to 50 percent.

As improvements in device design has allowed for lower pump volumes, there is interest in extending ventricular assist devices to high-risk populations (e.g., small infants and those with complex congenital heart disease) for whom the options for mechanical circulatory support are more limited. Ventricular assist devices as bridge to recovery and destination therapy are active areas of investigation in clinical trials and Pediatric Interagency Registry for Mechanical Circulatory Support (2018) analyses. Femoral vessel size limits the use of current U.S. Food and Drug Administration-approved percutaneous ventricular assist devices in small children.

Policy updates:

In 2017, we added three Pediatric Interagency Registry for Mechanically-Assisted Circulatory Support data analyses (Blume, 2016; Rosenthal, 2016; Rossano, 2016) and one evidence-based guideline update from the International Society for Heart and Lung Transplantation (Kirk, 2014) that addressed mechanical circulatory support in pediatric populations. Two of the analyses reported on characteristics and outcomes of 200 patients with a median age of 11 years (range 11 days to 18 years) and total follow-up of 783 patient-months, who underwent 222 durable ventricular assist device implants (Blume, 2016; Rosenthal, 2016). Rosano et al analyzed a subset of 109 patients supported with continuous-flow ventricular assist devices at 35 hospitals.

The majority of durable ventricular assist device recipients had an underlying disease of cardiomyopathy, underwent previous cardiac surgery or extracorporeal membrane oxygenation, had an Interagency Registry for Mechanically Assisted Circulatory Level 1 or 2 at the time of implant, and was supported primarily with a left ventricular assist device alone. Pulsatile-flow devices were used in 45 percent of cases and continuous-flow devices in 55 percent.

Actuarial survival ranged from 81 percent to 86 percent at six months (Blume, 2016; Rosenthal, 2016). The most frequent adverse events were device malfunction, infection, neurologic dysfunction, and bleeding, and most adverse events were likely to occur in the first 30 days. The overall rate of early (within 90 days of implantation) and late adverse events was 86.3 events per 100 patient-months and 20.4 events per 100
patient-months, respectively, which are comparable to adult outcomes (Rosenthal, 2016). At six months, continuous-flow ventricular assist devices as bridge to transplantation appear to have outcomes similar to those of adults, suggesting an expanding role for these devices in pediatric populations (Rossano, 2016).

Further study is needed to understand the impact of varying patient and device characteristics on outcomes in pediatric patients with the goal of improving adverse event rates and survival. These results and the updated guideline are consistent with our current policy, and no policy changes are warranted.

In 2018, we added one registry analysis of 147 patients with pre-transplant ventricular assist device support (index cohort) compared to 630 patients without pre-transplant ventricular assist device from the Pediatric Heart Transplant Study (Sutcliffe, 2018). There were no between-cohort differences in 1-year post-transplant survival (96 percent vs. 93 percent, \( P = .3 \)), freedom from infection (81 percent vs. 79 percent, \( P = .9 \)) or freedom from rejection (71 percent vs. 74 percent, \( P = .87 \)). Their results suggest that ventricular-assist device used as bridge to transplantation mitigates the severity of illness in pediatric patients who require heart transplantation. These results confirm the value of ventricular assist devices as a bridge to transplantation in pediatric populations, and no policy changes are warranted. The policy ID was changed from CP# 04.02.07 to CCP.1250.

In 2019, we removed ventricular assist devices from the policy. The coverage policy will focus solely on the total artificial heart, for which we identified no new information to add.

**References**

**Professional society guidelines/other:**


Peer-reviewed references:


**Centers for Medicare & Medicaid Services National Coverage Determinations:**

20.9 Artificial Hearts and Related Devices.
20.9.1 Ventricular Assist Devices.

**Local Coverage Determinations:**

A53986 Percutaneous Ventricular Assist Device.
A53988 Percutaneous Ventricular Assist Device.
A54910 Ventricular Assist Device (VAD) Supply or Accessory.

**Appendix**

New York Heart Association Functional Classification of Heart Failure (1994):

- **Class I.** No symptoms and no limitation in ordinary physical activity, e.g., shortness of breath when walking, climbing stairs etc.
- **Class II.** Mild symptoms (mild shortness of breath and/or angina) and slight limitation during ordinary activity.
- **Class III.** Marked limitation in activity due to symptoms, even during less-than-ordinary activity, e.g., walking short distances (~ up to 300 feet). Comfortable only at rest.
- **Class IV.** Severe limitations. Experiences symptoms even while at rest. Mostly bedbound patients.

American College of Cardiology Foundation/American Heart Association Stages of Heart Failure (Hunt, 2009):

- **Stage 1.** At high risk for heart failure but without structural heart disease or symptoms of heart failure.
- **Stage 2.** Structural heart disease but without signs or symptoms of heart failure.
- **Stage 3.** Structural heart disease with prior or current symptoms of heart failure.
Stage 4. Refractory heart failure requiring specialized interventions. Unable to carry on any physical activity without symptoms of heart failure, or symptoms of heart failure at rest.

Interagency Registry for Mechanically Assisted Circulatory profiles for classifying patients with advanced heart failure at time of implant (2018):

Profile 1. **Critical cardiogenic shock**, “crash and burn.”

Profile 2. **Progressive decline**, on inotropic support or in whom inotropic infusions cannot be maintained due to tachyarrhythmias, clinical ischemia or other intolerance.

Profile 3. **Stable but inotrope dependent**, or has a temporary circulatory support device after repeated documentation of failure to wean without symptomatic hypotension, worsening symptoms, or progressive organ dysfunction (usually renal).

Profile 4. **Resting symptoms** describes a patient who is at home on oral therapy but frequently has symptoms of congestion at rest or with activities of daily living.

Profile 5. **Exertion intolerant** living predominantly within the house or housebound.

Profile 6. **Exertion limited**, comfortable at rest without evidence of fluid overload and able to do some mild activity but easily fatigued with any meaningful physical exertion, and likely to have had a hospitalization for heart failure within the past year.

Profile 7. **Advanced New York Heart Association Class III**, clinically stable with a reasonable level of comfortable activity, despite history of previous decompensation that is not recent.