Cigna Medical Coverage Policy

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Subject **Total Artificial Heart**

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Hyperlink to Related Coverage Policies

Heart Transplantation
Ventricular Assist Devices (VADs) and Percutaneous Cardiac Support Systems

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Coverage Policy

Cigna covers the SynCardia temporary Total Artificial Heart (SynCardia Systems, Inc., Tucson, AZ) as medically necessary as a bridge to transplantation in individuals who are transplant-eligible and at risk of imminent death from biventricular failure.

Cigna does not cover the SynCardia temporary Total Artificial Heart for any other indication because it is considered experimental, investigational or unproven.

Cigna covers the AbioCor® Implantable Replacement Heart (ABIOMED™, Inc., Danvers, MA) as medically necessary as destination therapy when performed in accordance with the U.S. Food and Drug Administration's (FDA) Humanitarian Device Exemption (HDE) requirements when ALL of the following criteria are met:

- severe biventricular end stage heart disease
- not a cardiac transplant candidate
- age less than 75 years
- multiple inotropic support required
- not treatable by left ventricular assist device (LVAD) as destination therapy
- not weanable from biventricular support, if on such support
- none of the following contraindications:
  - presence of other irreversible end organ dysfunction that would compromise survival
  - inadequate psychosocial support
  - preoperative noninvasive anatomical assessment indicating inadequate fit (i.e., thoracic volume is unable to accommodate the device)

- presence of coagulation disorders

Cigna does not cover the AbioCor Implantable Replacement Heart for any other indication because it is considered experimental, investigational or unproven.

General Background

Heart failure can develop from any condition that overloads, damages, or reduces the efficiency of the heart muscle, impairing the ability of the ventricles to fill with or eject blood. Heart muscle may be damaged by myocardial infarction, coronary artery disease, infection, toxic chemical exposure, or years of untreated hypertension or heart valve abnormality. Treatment of heart failure includes pharmacologic interventions, including diuretics, angiotensin-converting enzyme inhibitors, vasodilators, digitalis, and beta-blockers. Pharmacologic therapy is ineffective in approximately 40% of heart failure patients, however. Heart transplantation is the most effective treatment for advanced heart failure, with most transplant centers achieving one-year survival rates of 85% or greater. Most transplant recipients can expect a ten-year survival of approximately 50%. The demand for donor hearts far exceeds the available supply, however. Cardiac transplant waiting lists have the highest mortality (30%) of any solid organ waiting list.

As patients become more hemodynamically compromised, there is an increased risk of death prior to transplantation, as well as a less favorable outcome following transplantation. External or implantable ventricular assist devices (VADs) are therefore used for many patients with end-stage heart failure while awaiting transplantation. Timely use of VADs may be successful in preventing further deterioration and reversing metabolic, cellular and nutritional compromise. The temporary use of these mechanical devices is referred to as "bridging" to transplant. VADs are usually inadequate as a bridge to transplant for patients with severe biventricular disease, and two paracorporeal devices may be needed. VADs may be contraindicated, however, in those with aortic regurgitation, cardiac arrhythmias, left ventricular thrombus, aortic prosthesis, acquired ventricular septal defect, or irreversible biventricular failure. A total artificial heart (TAH) is a mechanical circulatory device that has been used primarily to maintain patients until a suitable donor heart is available for transplantation, when VADs and biventricular assist devices are A fully implantable heart may also be considered as a permanent cardiac replacement, or "destination therapy", for patients with end-stage heart disease who are not candidates for heart transplantation (ECRI, 2012, Copeland et al., 2004, Bartoli, 2011).

U.S. Food and Drug Administration (FDA)
SynCardia temporary Total Artificial Heart (SynCardia Systems, Inc., Tucson, AZ): The SynCardia temporary Total Artificial Heart, formerly referred to as the CardioWest™ Total Artificial Heart**,** received FDA premarket approval (PMA) on October 15, 2004 as a bridge to transplant in cardiac transplant-eligible candidates at risk of imminent death from biventricular failure. The FDA approval states that the temporary TAH is intended to be used inside the hospital. The CardioWest TAH is a biventricular, pneumatic pulsatile blood pump that fully replaces the patient's ventricles and all four cardiac valves.

In the U.S.,the Syncardia TAH is powered by a large console on wheels that requires inpatient hospitalization, although in Europe, portable drivers are may be used (refer to section below, Use Outside the U.S.). A clinical trial is underway in the United States to evaluate the SynCardia Freedom Driver System in clilnically stable cardiac treansplant-eligible candidates who are implanted with the TAH. The trial began in March 2010, with an estimated completion date of October 2013.

AbioCor® Implantable Replacement Heart (IRH) (ABIOMED™, Inc., Danvers, MA): The AbioCor IRH is an artificial heart with completely internal components designed to provide circulatory control in order to prolong life and provide an acceptable quality of life. The internal components of the AbioCor system consist of the thoracic unit, implanted controller, implanted battery, and implanted transcutaneous energy transfer (TET) coil. The external components include the console and patient-carried electronics. The controller monitors and controls functioning of the device, including the pumping rate of the heart. The internal battery allows the recipient to be free from all external connections for up to one hour. The system also includes two external batteries that allow up to two hours of freedom of movement. When the patient is sleeping, or when the batteries are being recharged, the system is plugged into an electrical outlet (Samuels and Dowling, 2003; U.S. FDA, 2006).

The AbioCor IRH received FDA Humanitarian Device Exemption (HDE) approval on September 5, 2006, for use in severe biventricular end stage heart disease patients who are not cardiac transplant candidates and who:

- are less than 75 years old
- require multiple inotropic support
- are not treatable by LVAD destination therapy, and
- are not weanable from biventricular support, if on such support

The FDA Summary of Safety and Probable Benefit includes the following contraindications:

- Presence of other irreversible end organ dysfunction that would compromise survival
- Inadequate psychosocial support
- Preoperative noninvasive anatomical assessment indicating inadequate fit (i.e. thoracic volume is unable to accommodate the device)
- Presence of coagulation disorders

In order to receive HDE approval, a manufacturer must first be granted a Humanitarian Use Device (HUD) exemption by demonstrating that the device is designed to treat or diagnose a disease or condition that affects fewer than 4,000 people in the U.S. per year. Although data demonstrating the safety and probable clinical benefit are required for HDE approval, clinical trials evaluating the effectiveness of the device are not required. Following HDE approval, the hospital or healthcare facility institutional review board (IRB) must also approve the use of the device at that institution before it may be used in a patient. The regulatory basis for approving an HDE is that the device must not pose an unreasonable risk of illness or injury and the probable benefit of the device must outweigh the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. In the AbioCor HDE Summary of Safety and Probable Benefit, the FDA explained its decision to grant an HDE, stating that the preclinical, animal and clinical data all demonstrated that the device is able to achieve the desired level of cardiac support. Although the clinical study results indicated a concern regarding long-term reliability, changes have been made to the device that the FDA believes will improve reliability and durability. In determining whether the benefit of the device outweighs the risk, the FDA also took into account currently available devices and alternate treatments, determining that this is a patient population for whom there is no other treatment option. The FDA summary also states that, in order to address concerns with inadequate anticoagulation, AbioCor has established an anticoagulation committee which proposed a revised anticoagulation protocol to be used in the post-approval study.

The FDA HDE approval includes a requirement for a post-approval study to follow the first 25 patients implanted with the AbioCor IRH until death while on the device, or other outcome (e.g., elective termination by family, device malfunction, etc.). The post-approval study continues, with the latest report submitted in April 2012.

Literature Review

SynCardia temporary Total Artificial Heart): Kirsch et al. (2013) conducted a retrospective analysis of demographics, clinical characteristics, and survival of 90 patients bridged to transplantation using the SynCardia t-TAH at a single institution in France between 2000 and 2010. All patients were in cardiogenic shock secondary to idiopathic or ischemic cardiomyopathy or other causes. Prior to implantation, seven patients had cardiac arrest, 27 were on ventilators, and 18 were on extracorporeal life support. The mean duration of support was 84 ± 102 days. Thirty-five patients died while on support after a mean of 62 ± 107 days, respectively. Actuarial survival on the device at 30, 60, and 180 days after implantation was 74% ± 5%, 63% ± 6%, and 47% ± 8%, respectively. Nine patients experienced a stroke while on suppot, 13 had mediastinitis, and 35 required surgical exploration for bleeding, hematoma or infection.Twelve patients were discharged home, with mobile or portable drivers. Older recipient age and preoperative mechanical ventilation were found to be risk factors for death while on support. Fifty-five patients were transplanted after a mean of 97 ± 98 days of support. Actuarial survival rates were 78% ± 6%, 71% ± 6%, and 63% ± 8% at one, five, and eight years after transplantation. The authors stated that post-transplant survival was similar to that of patients undergoing primary heart transplantation in France.

A case series by Copeland et al. (2012) reported results of SynCardia TAH implantation as a bridge to transplant in 101 consecutive patients from 1993 to 2009 at University Medical Center in Tucson AZ. Sixty five of these patients had previously been reported as part of an institutional investigational device exemption study from 1993-2002 (Copeland et al., 2004, discussed below). Ninety-five percent of patients were Interagency

Registry for Mechanically Assisted Circulatory Support (INTERMACS) I. INTERMACS established seven different profiles for patients being implanted with mechanical circulatory support, ranging from INTERMACS 7, indicating advanced NYHA class III patients, through INTERMACS 1, acute decompensation (Irwin and Rippe, 2011). The mean support time was 87 days (median 53 days, range 1-44 days). Adverse events included stroke (7.9%) and re-operation for hemorrhage (24.7%). The survival to transplantation rate was 68.3%. The causes of death of 32 patients on device support included multiple organ failure (13), pulmonary failure (6) and neurologic injury (4). Survival following transplantation at one, five, and ten years was 76.8%, 60.5%, and 41.2%, respectively. At the time of publication, the longest term survivor was alive16.4 years post-implantation.

Roussel et al. (2009) evaluated comorbidity and survival of patients who received circulatory support with a CardioWest TAH (currently referred to as the SynCardia temporary Total Artificial Heart) while awaiting heart transplantation from 1990–2006 (n=42, 40 men, 2 women) at a single center in France. All patients were in cardiogenic shock despite maximum inotropic support at the time of implantation. Idiopathic or dilated cardiomyopathy was diagnosed in 19 patients and ischemic cardiomyopathy in 18 patients. Other diagnoses included postcardiotomy heart failure, fulminant myocarditis, and primary graft failure-rejection. Fourteen patients were receiving intra-aortic balloon pump support, six were receiving mechanical ventilation, and six had undergone cardiopulmonary resuscitation within the previous 24 hours. The duration of support was 1–292 days (mean 101 ± 86 days). Twelve patients died (28.5%) while receiving device support. Causes of death included multi organ failure, sepsis, acute respiratory distress syndrome, and alveolar hemorrhage. Thirty patients underwent transplantation. Actuarial survival rates for transplanted patients at one, five, and ten years were 90% (n=25) 81% (n=14) and 76% (n=10), respectively. Adverse events included stroke in three patients and infections in 35 patients. Significant device malfunctions occurred in four patients, but no malfunctions led to patient death.

Drakos et al. (2006) conducted a retrospective review of 278 patients who had undergone cardiac transplantation between 1993 and 2002. The study assessed the influence of pre-transplant mechanical cardiac support (MCS) on post-transplant outcomes. The authors stated that MCS before heart transplantation was previously associated with worse post-transplant outcomes than when MCS was not required. The study was intended to test the hypothesis that similar outcomes are now seen, regardless of whether MCS is required, due to changes in technology, expertise, patient selection, and timing of transplantation. Of the 278 patients included in the analysis, 72 had required MCS and 206 patients had not. Six of the 72 patients who required MCS received the CardioWest TAH. One month and one year survival did not differ between the groups (MCS 92% and 85%, respectively; no MCS 97% and 92%, respectively. The percentage of patients free from rejection at one year was also similar (MCS: 52%, no MCS: 52%, p=0.60). The incidence of chronic renal insufficiency was lower in the MCS group (15.3% vs. 37.9%, p=.001).

FDA approval of the CardioWest TAH (currently referred to as the SynCardia temporary Total Artificial Heart) was based on a multicenter controlled clinical trial that demonstrated improved survival rates in selected patients who received the TAH as a bridge to transplant (n=81) compared to a historical control group (n=35) who received a transplant without previous mechanical circulatory support (Copeland, et al., 2004). The primary endpoints of the study included the rates of survival to heart transplantation and of survival after transplantation. All patients were candidates for transplant and were at risk of imminent death from irreversible biventricular failure. The mean time from entry in the study to transplant was 79.1 days for the TAH group and 8.5 days for the control group. A greater percentage of patients in the TAH group survived to transplant than in the control group (79% vs. 46%, respectively). Overall, one-year survival was 70% in the TAH group and 31% in the control group. The survival rates at one and five years after transplantation in the TAH group were 86% and 64%, respectively, compared to 69% and 34% in the control group. Treatment success was achieved in 69% of the patients in the TAH group, compared to 37% in the control group.

An earlier study of one French center's fifteen-year experience with the Jarvik-7/CardioWest TAH (Leprince, et al., 2003) concluded that the device was a safe and efficient bridge for patients with terminal congestive heart failure awaiting cardiac transplantation. Between 1986 and 2001, 127 patients were bridged to transplantation with the TAH. All were in terminal biventricular failure despite maximum inotropic support. Patients were divided into two groups. Those in Group I had cardiac failure caused by idiopathic or ischemic dilated cardiomyopathy, while those in Group II had cardiac failure caused by diseases of miscellaneous origin. For the most recent period (1998–2001), 74% of patients in Group I received transplants. Survival on the TAH was not as successful for the more difficult patients in Group II, with 50% of patients receiving transplants.

Several published uncontrolled and nonrandomized controlled clinical trials conducted in heart transplantation centers also concluded that the SynCardia TAH was relatively safe and effective as a bridge to transplantation in carefully selected heart transplant candidates (Copeland, et al., 1996, 1998, 1999, 2001; Arabia, et al., 1997).

AbioCor Implantable Replacement Heart (IRH): Dowling et al. (2004) published early results of a multisite feasibility clinical trial evaluating the AbioCor IRH in the treatment of severe, irreversible biventricular heart failure. Patients considered for inclusion in the trial were adults with biventricular failure at maximal medical therapy and dependence on inotropes or inability to tolerate inotropes due to arrhythmia. Patients were excluded if they were candidates for other therapy, including heart transplantation, or had a predicted survival of greater than 30% at 30 days. Additional exclusion criteria included end-organ dysfunction believed to be irreversible, active infection, severe peripheral vascular disease, blood dyscrasia, or recent stroke or transient ischemic attack caused by atherosclerotic disease. Dowling reported on the initial seven adult male patients included in the study. All were in cardiogenic shock despite maximal medical therapy, including intra-aortic balloon pumps. The mean age was 66.7 ± 10.4 years. One intraoperative death occurred due to bleeding, and one early death was caused by a reaction to aprotinin, an intravenously administered protein which helps prevent bleeding following cardiac surgery. There were multiple morbidities related to the severity of illness prior to implantation: five had prolonged intubation; two had hepatic failure (resolved in one); four had renal failure (resolved in three); and one each had recurrent gastrointestinal bleeding, acute cholecystitis requiring laparotomy, respiratory failure that resolved after three days, and malignant hyperthermia that resolved. Three late deaths occurred—one due to multiple system organ failure on postoperative day 56, and one was caused by a cerebrovascular accident (CVA) on postoperative day 142. The latter patient was unable to tolerate anticoagulation. The two patients who had large CVAs were found to have thrombus on the atrial cage struts. These struts were removed for future implants. There was no significant hemolysis or device-related infection. Three patients were able to take multiple trips out of the hospital, and two patients were discharged from the hospital.

Additional results of the AbioCor clinical trial are included in the FDA HDE Summary of Safety and Probable Benefit (2006). The trial was conducted between July 2001 and November 2004. Fourteen patients, including the seven patients included in the previously published early results, were implanted with the device. Twelve of the fourteen patients survived surgery. The mean individual survival time for all 14 patients was 4.5 months, ranging from 0–512 days. The median was 3.6 months. Major adverse events included transient ischemic attack (TIA), surgical bleeding (e.g., tamponade), nonsurgical bleeding, infection unrelated to the device, and respiratory complications. Neurologic, renal, and hepatic complications also occurred. The tendency for bleeding was high; 10 of 12 patients could not tolerate the recommended level of anticoagulation more than 60% of the time, and of these 10, seven could not tolerate it more than 80% of the time. All of the 12 patients who survived the surgery lived the remainder of their lives on the device. Support to six of the 12 was withdrawn secondary to CVAs. There were two device failures. Four patients died of multi-organ failure or sepsis. Of the 12 patients who survived surgery, 10 lived for more than 60 days and were able to interact with family members. Four of these 10 patients had out-of-hospital activities, and the remaining six patients experienced varying degrees of recovery, including walking and in-hospital excursions.

Of the 14 patients, nine completed the Minnesota Living with Heart Failure quality-of-life questionnaire pre-and post-implant. All were assessed at least once between one and three months post-implant, and 7 of 9 were reported to show improvement in quality of life for at least one time point after implantation. The study did not report how long the improved QOL was maintained, however, or what percentage of patients improved over baseline levels. This small case series is the only study evaluating the AbioCor Implantable Replacement Heart published to date. Additional studies with larger numbers of patients are needed to fully evaluate outcomes, including adverse events, quality of life, and survival following implantation.

The FDA requires that Abiomed provide a comprehensive information package for patients and families that clearly describes the risks as well as the benefits of the device and explains what can be expected before, during and after surgery. Although not all eligible patients will choose this treatment, the AbioCor IRH provides an option for selected patients with biventricular heart failure who are not candidates for heart transplantation and have no other treatment options.

ECRI Emerging Technology Evidence Report
A 2012 ECRI evidence report evaluated total artificial hearts as a bridge to transplantation and destination therapy. The quality, quantity, and consistency of evidence were considered to be low.

The authors concluded that the evidence is currently insufficient to determine whether a TAH as a bridge to transplantation improves survival and successful recovery compared to optimized medical therapy. Although one low-quality retrospectively controlled study suggests improved survival associated with TAH use, the control group was poorly matched and may have had a greater risk of death than the TAH group. The two groups had statistically significant baseline differences, and this selection bias has the potential to confound the comparison between the groups, particularly if the control group had a higher baseline risk of death. Because of the probable difficulty in recruiting patients into a prospective comparative trial, however, it is unlikely that higher-quality trials will ever be conducted to evaluate this technology.

The authors also concluded that there is insufficient evidence to determine whether a TAH as destination therapy improves patient-oriented outcomes in patients who are not candidates for transplantation. The 14 patients included in the only available study, a case series, were not considered candidates for heart transplantation and were unresponsive to optimal medical therapy. Based on estimated risk, these patients had at least a 70% probability of death within 30 days in the absence of the AbioCor device, so it was considered a treatment of last resort. Ten of 14 patients survived 60 days, but the percentage of patients that met the goal of survival without unacceptable deficits is unclear. Although the average patient survival time was longer than the expected survival time without TAH implantation, it is not possible to determine whether the patients would have survived longer than expected without a TAH.

Professional Societies/Organizations
Heart Failure Society of America (HFSA): The following recommendation is included in the 2010 Comprehensive Heart Failure Practice Guideline (Lindenfeld, et al.):

- Patients awaiting heart transplantation who have become refractory to all means of medical circulatory support should be considered for a mechanical support device as a bridge to transplant. (Strength of Evidence = B).

Strength of evidence B is described as evidence arising from cohort studies or smaller clinical trials with physiologic or surrogate endpoints. The mechanical support devices mentioned in the guideline text include the CardioWest TAH and several LVADs. The recommendation above does not make a distinction as to indications for use of a TAH versus an LVAD.

Use Outside of the U.S.
The Syncardia Total Artificial Heart received the CE mark on May 16, 2005, and a Class IV license with conditions by Health Canada on October 27, 2005, for use as a bridge to transplant in cardiac transplant-eligible candidates at risk of imminent death from biventricular failure.

The Freedom Driver System, a wearable portable driver, received the CE mark on March 4, 2010. This system replaces the large console typically used with the Syncardia heart, allowing stable patients in Europe to be discharged while awaiting a donor heart.

The 2013 International Society for Heart and Lung Transplantation Guidelines for Mechanical Circulatory Support (Feldman et al.) include the following recommendations pertinent to total artificial hearts.

Class IIa, Level of Evidence C

- Patients with complex congenital heart disease, atypical situs or residual intraventricular shunts who are not candidates for LV support should be considered for a total artificial heart (Class IIa, Level of evidence: C)
- Patients with treatment-refractory recurrent sustained ventricular tachycardia or ventricular fibrillation in the presence of untreatable arrhythmogenic pathologic substrate (e.g., giant cell myocarditis, scar, sarcoidosis), should not be considered for LV support alone, but rather biventricular support or a total artificial heart (Class IIa, Level of evidence: C)

A Class IIa recommendation indicates that the weight of evidence/opinion is in favor of usefulness/effiecacy. Level of evidence C indicates a consensus of opinion of the experts and/or small studies, retrospective studies, or registries.

Summary
Heart transplantation has become the standard treatment for eligible patients with irreversible biventricular failure unresponsive to medical treatment. The supply of donor hearts has decreased in recent years, however, while the demand has increased significantly. External or implantable ventricular assist devices (VADs) are therefore used for many patients with end-stage heart failure while awaiting transplantation. VADs may be contraindicated, however, in those with aortic regurgitation, cardiac arrhythmias, left ventricular thrombus, aortic prosthesis, acquired ventricular septal defect, or irreversible biventricular failure. A total artificial heart (TAH) may be used to maintain patients until a suitable donor heart is available for transplantation, when VADs and biventricular assist devices are contraindicated. There is adequate evidence to demonstrate that the SynCardia temporary Total Artificial Heart (SynCardia Systems, Inc., Tucson, AZ) is a relatively safe and effective bridge to transplantation in carefully selected heart transplant candidates who are at risk of imminent death due to biventricular failure.

The AbioCor® Implantable Replacement Heart (IRH) (Abiomed™ Inc., Danvers, MA) received a U.S. Food and Drug Administration (FDA) Humanitarian Device Exemption (HDE) in 2006. The AbioCor IRH may be a treatment option for carefully selected patients with severe biventricular end-stage heart disease who are not cardiac transplant candidates, are less than 75 years old, require multiple inotropic support, are not treatable by left ventricular assist device (LVAD) destination therapy, and are not weanable from biventricular support, if on such support.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

Covered when medically necessary:

CPT®* Codes	**Description**
0051T	Implantation of a total replacement heart system (artificial heart) with recipient cardiectomy
0052T	Replacement or repair of thoracic unit of a total replacement heart system (artificial heart)
0053T	Replacement or repair of implantable component or components of total replacement heart system (artificial heart) excluding thoracic unit

***Current Procedural Terminology (CPT®) ©2012 American Medical Association: Chicago, IL.**

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