Total Artificial Hearts and Implantable Ventricular Assist Devices

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Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services Are Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:
- Benefits are available in the member’s contract/certificate, and
- Medical necessity criteria and guidelines are met.

Post-cardiotomy Setting/Bridge to Recovery
Based on review of available data, the Company may consider implantable ventricular assist devices (VADs) with U.S. Food and Drug Administration (FDA) approval or clearance in the postcardiotomy setting in patients who are unable to be weaned off cardiopulmonary bypass to be eligible for coverage.

Bridge to Transplantation
Based on review of available data, the Company may consider implantable ventricular assist devices (VADs) with U.S. Food and Drug Administration (FDA) approval or clearance as a bridge to heart transplantation for patients who are currently listed as heart transplantation candidates and not expected to survive until a donor heart can be obtained, or are undergoing evaluation to determine candidacy for heart transplantation to be eligible for coverage.

Based on review of available data, the Company may consider implantable ventricular assist devices (VADs) with U.S. Food and Drug Administration (FDA) approval or clearance, including humanitarian device exemptions, as a bridge to heart transplantation in children 16 years old or younger who are currently listed as heart transplantation candidates and not expected to survive until a donor heart can be obtained, or are undergoing evaluation to determine candidacy for heart transplantation to be eligible for coverage.

Based on review of available data, the Company may consider total artificial hearts (TAHs) with U.S. Food and Drug Administration (FDA)-approved devices as a bridge to heart transplantation for patients with biventricular failure who have no other reasonable medical or surgical treatment options, who are ineligible for other univentricular or biventricular support devices, and are currently listed as heart transplantation candidates or are undergoing evaluation to determine candidacy for heart transplantation, and not expected to survive until a donor heart can be obtained to be eligible for coverage.

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:
- Benefits are available in the member’s contract/certificate, and
- Medical necessity criteria and guidelines are met.
Destination Therapy
Based on review of available data, the Company may consider implantable ventricular assist devices (VADs) with U.S. Food and Drug Administration (FDA) approval or clearance may be considered medically necessary as destination therapy with end-stage heart failure patients who are ineligible for human heart transplant and who meet the following "REMATCH Study" criteria to be eligible for coverage.

Patient Selection Criteria
Coverage eligibility will be considered when the following criteria are met:

- New York Heart Association (NYHA) class IV heart failure for ≥ 60 days, or patients in NYHA class III/IV for 28 days, received ≥ 14 days’ support with intra-aortic balloon pump (IABP) or dependent on IV inotropic agents, with two failed weaning attempts.

In addition, patients must not be candidates for human heart transplant for one or more of the following reasons:

- Age > 65 years; or
- Insulin-dependent diabetes mellitus with end-organ damage; or
- Chronic renal failure (serum creatinine > 2.5 mg/dL for ≥ 90 days; or
- Presence of other clinically significant condition

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Other Indications
Based on review of available data, the Company considers other applications of implantable ventricular devices or total artificial hearts (TAHs) including, but not limited to, the use of total artificial hearts (TAHs) as destination therapy. The use of non-U.S. Food and Drug Administration (non-FDA) approved or cleared implantable ventricular assist devices (VADs) or total artificial hearts (TAHs) is considered to be investigational.*

Based on review of available data, the Company considers percutaneous ventricular assist devices (pVADs) for all indications to be investigational.*

Background/Overview
Heart failure may be the consequence of a number of differing etiologies, including ischemic heart disease, cardiomyopathy, congenital heart defects, or rejection of a heart transplant. The reduction of cardiac output is considered to be severe when systemic circulation cannot meet the body’s needs under minimal exertion. Heart transplantation improves quality of life and has survival rates at 1, 5, and 10 years of 88%, 74%, and 55%, respectively. The supply of donor organs has leveled off, while candidates for transplants are increasing, compelling the development of mechanical devices.

Initial research into mechanical assistance for the heart focused on the TAH, a biventricular device which completely replaces the function of the diseased heart. An internal battery required frequent recharging.
from an external power source. Many systems use a percutaneous power line, but a transcutaneous power-transfer coil allows for a system without lines traversing the skin, possibly reducing the risk of infection. Because the heart must be removed, failure of the device is synonymous with cardiac death.

A fully bioprosthetic TAH, which is fully implanted in the pericardial sac and is electrohydrodynamically actuated, has been developed and tested in 2 patients, but is currently experimental.

**Ventricular Assist Devices**

Implantable VADs are attached to the native heart, which may have enough residual activity to withstand a device failure in the short term. In reversible conditions of heart failure, the native heart may regain some function, and weaning and explanting of the mechanical support system after months of use has been described. VADs can be classified as internal or external, electrically or pneumatically powered, and pulsatile or continuous flow. Initial devices were pulsatile, mimicking the action of a beating heart. More recent devices may use a pump, which provides continuous flow. Continuous devices may move blood in rotary or axial flow.

At least 1 VAD system developed is miniaturized and generates an artificial pulse, the HeartMate 3 Left Ventricular Assist System.

Surgically implanted VADs represent a method of providing mechanical circulatory support for patients not expected to survive until a donor heart becomes available for transplant or for whom transplantation is otherwise contraindicated or unavailable. VADs are most commonly used to support the left ventricle, but right ventricular and biventricular devices may be used. The device is larger than most native hearts, and therefore the size of the patient is an important consideration: the pump may be implanted in the thorax or abdomen or remain external to the body. Inflow to the device is attached to the apex of the failed ventricle, while outflow is attached to the corresponding great artery (aorta for left ventricle, pulmonary artery for right ventricle). A small portion of ventricular wall is removed for insertion of the outflow tube; extensive cardiotomy affecting the ventricular wall may preclude VAD use.

**Percutaneous Ventricular Assist Devices**

Devices in which most of the system’s components are external to the body are for short-term use (6 hours to 14 days) only, due to the increased risk of infection and need for careful, in-hospital monitoring. Some circulatory assist devices are placed percutaneously (ie, are not implanted). These may be referred to as pVADs. pVADs are placed through the femoral artery. Two different pVADs have been developed, the TandemHeart™ (Cardiac Assist™; Pittsburgh, PA), and the Impella® device (Abiomed™; Aachen, Germany). In the TandemHeart system, a catheter is introduced through the femoral vein and passed into the left atrium via transseptal puncture. Oxygenated blood is then pumped from the left atrium into the arterial system via the femoral artery. The Impella device is introduced through a femoral artery catheter. In this device, a small pump is contained within the catheter that is placed into the left ventricle. Blood is pumped from the left ventricle, through the device, and into the ascending aorta. Adverse events associated with pVAD include access site complications such as bleeding, aneurysms, or leg ischemia. Cardiovascular complications can also occur, such as perforation, myocardial infarction, stroke, and arrhythmias.
There are several situations in which pVADs may offer possible benefits: (1) cardiogenic shock that is refractory to medications and IABP, (2) cardiogenic shock, as an alternative to IABP, and (3) high-risk patients undergoing invasive cardiac procedures who need circulatory support.

IABPs are outside the scope of this policy.

**FDA or Other Governmental Regulatory Approval**

U.S. FDA

A number of mechanical circulatory support devices have received approval or clearance for marketing by FDA. These devices are summarized in Table 1, and described further in following sections.

**Table 1. Available Mechanical Circulatory Support Devices**

<table>
<thead>
<tr>
<th>Device</th>
<th>Manufacturer</th>
<th>Date of Initial Approval</th>
<th>Method of FDA Clearance</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventricular assist devices</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thoratec IVAD</td>
<td>Thoratec</td>
<td>Aug 2004</td>
<td>PMA supplement</td>
<td>Bridge to transplant and postcardiectomy</td>
</tr>
<tr>
<td>DeBakey VAD Child</td>
<td>MicroMed</td>
<td>Apr 2004</td>
<td>HDE</td>
<td>Bridge to transplant in children 5-16 y of age</td>
</tr>
<tr>
<td>HeartMate II</td>
<td>Thoratec</td>
<td>Apr 2008</td>
<td>PMA</td>
<td>Bridge to transplant and destination</td>
</tr>
<tr>
<td>Centrimag</td>
<td>Levitronix</td>
<td>Oct 2008</td>
<td>HDE</td>
<td>Postcardiomy</td>
</tr>
<tr>
<td>Berlin Heart EXCOR Pediatric VAD</td>
<td>Berlin</td>
<td>Dec 2011</td>
<td>HDE</td>
<td>Bridge to transplant</td>
</tr>
<tr>
<td>HeartWare Ventricular Assist System</td>
<td>HeartWare</td>
<td>Dec 2012</td>
<td>PMA</td>
<td>Bridge to transplant</td>
</tr>
<tr>
<td>Percutaneous ventricular assist devices</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Impella</td>
<td>Abiomed</td>
<td>May 2008</td>
<td>510(k)</td>
<td>Partial circulatory support using extracorporeal bypass control unit for periods up to 6 h</td>
</tr>
<tr>
<td>TandemHeart</td>
<td>Cardiac Assist</td>
<td>Sep 2005</td>
<td>510(k)</td>
<td>Temporary left ventricular bypass of ≤6 h</td>
</tr>
</tbody>
</table>

FDA: U.S. FDA; HDE: humanitarian device exemption; PMA: premarket approval.

**Total Artificial Heart**

In October 2004, device CardioWest™ Temporary Total Artificial Heart (SynCardia Systems, Tucson, AZ) was approved by FDA through the premarket approval process (PMA) for use as a bridge to transplant in cardiac transplant-eligible candidates at risk of imminent death from biventricular failure. Also, the temporary CardioWest Total Artificial Heart (TAH-t) is intended for use inside the hospital. In April 2010, FDA approved a name change to SynCardia Temporary Total Artificial Heart. FDA product code: LOZ.

In September 2006, the AbioCor® Implantable Replacement Heart System (AbioMed, Danvers MA) was approved by FDA through the HDE process for use in severe biventricular end stage heart disease patients who are not cardiac transplant candidates and who:

- Are younger than 75 years of age;
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- 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.

In addition to meeting other criteria, patients who are candidates for the AbioCor TAH must undergo a screening process to determine if their chest volume is large enough to hold the device. The device is too large for approximately 90% of women and for many men. FDA HDE: H040006.

Ventricular Assist Devices
In December 1995, the Thoratec® Ventricular Assist Device System (Thoratec Corp., Pleasanton, CA) was approved by FDA through the PMA process for use as a bridge to transplantation in patients suffering from end stage heart failure. The patient should meet all of the following criteria:
- Candidate for cardiac transplantation,
- Imminent risk of dying before donor heart procurement, and
- Dependence on, or incomplete response to, continuous vasopressor support.

In May 1998, supplemental approval for this device was given for the indication for postcardiotomy patients who are unable to be weaned from cardiopulmonary bypass. In June 2001, supplemental approval was given for a portable external driver to permit excursions within a 2-hour travel radius of the hospital in the company of a trained caregiver. In November 2003, supplemental approval was given to market the device as Thoratec Paracorporeal VAD. In August 2004, supplemental approval was given to a modified device to be marketed as the Thoratec Implantable VAD for the same indications. In January 2008, supplemental approval was given to delete Paracorporeal VAD use.

In February 2004, FDA approved the DeBakey VAD® Child under the HDE approval process. According to FDA, this device is indicated under HDE for both home and hospital use for children between the ages of 5 and 16 years who have end stage ventricular failure requiring temporary mechanical blood circulation until a heart transplant is performed.

In April 2008, continuous flow device HeartMate® II LVAS (Thoratec, Pleasanton, CA) was approved by FDA through the PMA process for use as a bridge to transplantation in cardiac transplant candidates at risk of imminent death from nonreversible left ventricular failure. The HeartMate II LVAS is intended for use both inside and outside the hospital. In January 2010, the device received the added indication as destination therapy for use in patients with New York Heart Association class IIIB or IV end-stage left ventricular failure who have received optimal medical therapy for at least 45 of the last 60 days and are not candidates for cardiac transplantation.

In October 2008, device Centrimag® Right Ventricular Assist Device (Levitronix, Zurich) was approved by FDA under the HDE to provide temporary circulatory support for up to 14 days for patients in cardiogenic shock due to acute right-sided heart failure.
In December 2011, the Berlin Heart EXCOR™ Pediatric VAD was approved via HDE. The indications for this device are pediatric patients with severe isolated left ventricular or biventricular dysfunction who are candidates for cardiac transplant and require circulatory support.

In December 2012, FDA approved the HeartWare™ Ventricular Assist System (HeartWare, Miami Lakes, FL) through PMA. The device is approved as a bridge to cardiac transplantation in patients at risk for death from refractory end stage left ventricular heart failure.

FDA product code: DSQ.

Percutaneous Ventricular Assist Devices (Circulatory Assist Devices)

In May 2008, the Impella™ Recover LP 2.5 Percutaneous Cardiac Support System (Abiomed, Aachen, Germany) was cleared for marketing by FDA through the 510(k) process for short-term (<6 hours) use in patients requiring circulatory support.

In March 2015, the Impella 2.5 System received approval through the PMA process for temporary ventricular support during high-risk percutaneous coronary interventions.

The TandemHeart™ (Cardiac Assist, Pittsburgh) received a similar 510(k) approval for short-term circulatory support in September 2005. FDA product code: KFM.

Several other devices are in clinical trials or awaiting FDA review.

Centers for Medicare and Medicaid Services (CMS)

Medicare has a national coverage determination for artificial hearts and related devices, including VADS.

The national coverage policy mandates coverage for VADs in the post-cardiotomy setting as long as the following conditions are met:

- The VAD has approval from FDA for post-cardiotomy support.
- The VAD is used according to the FDA-approved labeling instructions.

The national coverage policy also mandates coverage for VADs as a bridge-to-transplant as long as the following conditions are met:

- The VAD has approval from FDA for the bridge-to-transplant indication.
- The VAD is used according to the FDA-approved labeling instructions.
- The patient is approved and listed as a candidate for heart transplantation by a Medicare-approved heart transplant center.
- The implanting site, if different than the Medicare-approved transplant center, must receive written permission from the Medicare-approved heart transplant center under which the patient is listed prior to implantation of the VAD.

The national coverage policy mandates coverage for VADs as destination therapy as long as the following conditions are met:
The VAD has approval from FDA for the destination therapy indication.

Patient selection: VADs are covered for patients who have chronic end-stage heart failure (New York Heart Association class IV end-stage left ventricular failure) who are not candidates for heart transplantation, and meet all of the following conditions:

- Have failed to respond to optimal medical management (including beta-blockers and ACE inhibitors if tolerated) for at least 45 of the last 60 days, or have been balloon pump-dependent for 7 days, or IV inotrope-dependent for 14 days; and,
- Have a left ventricular ejection fraction (LVEF) <25%, and,
- Have demonstrated functional limitation with a peak oxygen consumption of ≤14 mL/kg/min unless balloon pump- or inotrope-dependent or physically unable to perform the test.

Facility criteria: As of an October 30, 2013, decision memo on a National Coverage Analysis for VADs, the CMS concluded that the evidence is sufficient to conclude that VADs implanted in facilities that meet certain criteria improve health outcomes. Facilities currently credentialed by the Joint Commission for placement of VADs as DT [destination therapy] may continue as Medicare-approved facilities until October 30, 2014. At the conclusion of this transition period, these facilities must be in compliance with the following criteria as determined by a credentialing organization. As of the effective date, new facilities must meet the following criteria as a condition of coverage of this procedure:

- Beneficiaries receiving VADs for DT must be managed by an explicitly identified cohesive, multidisciplinary team of medical professionals with the appropriate qualifications, training, and experience. The team embodies collaboration and dedication across medical specialties to offer optimal patient-centered care. Collectively, the team must ensure that patients and caregivers have the knowledge and support necessary to participate in shared decision making and to provide appropriate informed consent. The team members must be based at the facility and must include individuals with experience working with patients before and after placement of a VAD. The team must include, at a minimum, all of the following:
  - At least one physician with cardiothoracic surgery privileges and individual experience implanting at least 10 durable, intracorporeal, left ventricular VADs as BTT [bridge to transplant] or DT over the course of the previous 36 months with activity in the last year.
  - At least one cardiologist trained in advanced heart failure with clinical competence in medical and device-based management including VADs, and clinical competence in the management of patients before and after heart transplant.
  - A VAD program coordinator.
  - A social worker.
  - A palliative care specialist.
- Facilities must be credentialed by an organization approved by CMS.

The national coverage policy mandates coverage for artificial hearts as bridge to transplant or destination therapy when performed under coverage with evidence development when a clinical study meets the criteria outlined in the Medicare policy and addresses one of the following questions:

- Were there unique circumstances such as expertise available in a particular facility or an unusual combination of conditions in particular patients that affected their outcomes?
Rationale/Source

The most recent literature review was performed for the period up to April 21, 2015. The literature review focuses on 3 types of devices: (1) LVADs, (2) TAHs, and (3) pVADs. The literature review addresses short-term use of the devices as a bridge to recovery or transplantation. LVADs and TAHs are also evaluated as longer term destination therapy for patients who are not transplant candidates. Following is a summary of the key literature to date.

Ventricular Assist Devices

VADs as Bridge to Recovery

VADs may have a role in bridging patients to recovery, particularly if there is reverse remodeling of the left ventricle.

In 2016, Acharya et al reported on patients who underwent VAD placement for acute myocardial infarction (AMI) who were enrolled in the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) registry, a prospective national registry of FDA-approved durable mechanical circulatory support devices. Patients who had an AMI as the admitting diagnosis or a major myocardial infarction (MI) as a hospital complication that resulted in VAD implantation (n=502) were compared with patients who underwent VAD implantation for non-AMI indications (n=9727). Patients in the AMI group were generally sicker at baseline, with higher rates of smoking, severe diabetes, and peripheral vascular disease, but had fewer cardiac surgeries and recent cardiovascular hospitalizations. Most AMI patients (53.8%) were implanted with a “bridge-to-candidacy” strategy. At 1 month post-VAD, 91.8% of the AMI group was alive with the device in place. At 1 year post-VAD, 52% of the AMI group were alive with the device in place, 25.7% had received a transplant, 1.6% had their VAD explanted for recovery, and 20.7% died with the device in place.

A number of relatively small, noncomparative studies have evaluated LVADs as bridge-to-recovery therapy. In a 2006 study, a series of 15 patients with severe heart failure due to nonischemic cardiomyopathy underwent implantation of LVADs, along with medical management designed to enhance myocardial recovery. Eleven of 15 patients had enough myocardial recovery to undergo LVAD explantation; 2 patients died after explantation. Among those who survived, the cumulative rate of freedom from recurring heart failure was 100% and 88.9%, respectively, at 1 and 4 years postexplantation. The same group subsequently reported results of their LVAD explantation protocol among patients with severe heart failure due to nonischemic cardiopathy who had nonpulsatile LVADs implanted. They included 20 patients who received a combination of angiotensin-converting enzyme inhibitors, β-blockers, and adosterol antagonists followed by the β₂-agonist clenbuterol. One patient, lost to follow-up, died after 240 days of support. Of the remaining 19 patients, 12 (63.2%) were successfully explanted after a mean 286 days; estimated survival without heart failure recurrence was 83.3% at 1 and 3 years. In a prospective multicenter study to assess myocardial recovery in patients with LVAD implantation as a bridge to transplant, Maybaum et al evaluated.
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67 patients with heart failure who had undergone LVAD implantation for severe heart failure. After 30 days, patients demonstrated significant improvements compared with their pre-LVAD state in left ventricular ejection fraction (LVEF; 17.1% vs 34.12%, p<0.001), left ventricular end-diastolic diameter (7.1 cm vs 5.1 cm, p<0.001), and left ventricular mass (320 g vs 194 g, p<0.001), respectively. However, only 9% of patients demonstrated sufficient recovery to have their LVAD explanted.

Takayama et al reported outcomes for a retrospectively defined cohort of 143 patients who received a CentriMag VAD as a "bridge to decision" for refractory cardiogenic shock due to a variety of causes. Patients were managed with a bridge-to-decision algorithm. Causes of cardiogenic shock included failure of medical management (n=71), postcardiotomy shock (n=37), graft failure post heart transplantation (n=2), and right ventricular failure postimplantable LVAD (n=13). The device configuration was biventricular in 67%, isolated right VAD in 26%, and isolated left VAD in 8%. After a mean duration of support of 14 days (interquartile range, 8-26 days), 30% of patients had myocardial recovery, 15% had device exchange to an implantable VAD, and 18% had a heart transplant.

In a smaller single-center retrospective cohort study, Mohamedali et al reported outcomes for 48 patients treated with biventricular support with the CentriMag device as a “bridge to decision”, 18 of whom had biventricular support with venoarterial (VA) extracorporeal membrane oxygenation (ECMO), while the remainder received just biventricular VAD support. Overall, 23 patients were explanted, 9 to recovery, 14 to a durable LVAD, with 3 additional patients explanted for withdrawal of care.

Section Summary
There has been interest in prospectively identifying subsets of patients who might benefit from a temporary VAD with the goal of bridging to recovery. Available studies have indicated that a subset of patients who receive a VAD as a bridge to transplant or as destination therapy have demonstrated improvements in their cardiac function, sometimes to the point that they no longer require the VAD. However, questions remain about defining and identifying the population most likely to experience cardiac recovery with VAD placement. One clearly defined population in which the potential for myocardial recovery exists is in the postcardiotomy setting. The current evidence is insufficient to allow identification of other heart failure patient populations who might benefit from the use of an LVAD as a specific bridge-to-recovery treatment strategy.

VADs as Bridge to Transplant

Efficacy
A 1996 TEC Assessment concluded that VADs can provide an effective bridge to transplantation. Goldstein et al published a more recent review. It should be recognized that VADs do not change the number of patients undergoing heart transplantation due to the fixed number of donor hearts. However, the VAD will categorize its recipient as a high-priority heart transplant candidate.

The available evidence on the efficacy of VADs in bridging patients with refractory heart failure to transplant includes single-arm series, which generally have reported high success rates in bridging to transplant.
In 2011, Strueber et al published a case series of 50 patients awaiting heart transplantation treated with HeartWare Ventricular Assist System, which is a smaller, continuous-flow centrifugal device implanted in the pericardial space. Patients were followed until transplantation, myocardial recovery, device explant, or death. The median duration of time on the VAD was 322 days. Nine patients died, 3 from sepsis, 3 from multiple organ failure, and 3 from hemorrhagic stroke. At the end of follow-up, 20 (40%) patients had undergone transplant, 4 (8%) had the pump explanted, and the remaining 17 (34%) continued on pump support. The most common complications were infection and bleeding: 21 (42%) patients had infections and 5 (10%) had sepsis, while 15 (30%) patients had bleeding complications, 10 (20%) of whom required surgery.

In 2012, Aaronson et al reported results of a multicenter, prospective study of a newer generation LVAD, the HeartWare. The study enrolled 140 patients awaiting heart transplantation who underwent HeartWare implantation. A control group of 499 subjects comprised patients drawn from the INTERMACS database, which collects data on patients who receive FDA-approved durable mechanical circulatory support devices. The study's primary outcome was defined as survival on the originally implanted device, transplantation, or explantation for ventricular recovery at 180 days. Secondary outcomes were comparisons of survival between groups and functional, quality of life (QOL), and adverse event outcomes in the HeartWare group. Success occurred in 90.7% of the HeartWare group and 90.1% of controls (p<0.001, noninferiority with a 15% margin). Serious adverse events in the HeartWare group included, most commonly, bleeding, infections, and perioperative right heart failure.

In 2013, Slaughter et al reported combined outcomes for patients included in the HeartWare bridge-to-transplant study previously described and a continued-access protocol granted by FDA. The study included 322 patients with heart failure, eligible for heart transplant, who received the HeartWare (140 patients from the original study; 190 patients in the continue-access protocol who were monitored to outcome or had completed 180 days of follow-up at the time of this analysis). Survival at 60, 180, and 360 days was 97%, 91%, and 84%, respectively. The most common adverse events were respiratory dysfunction, arrhythmias, sepsis, and driveline exit site infections. Patients generally had improvements in quality-of-life measures.

In 5 reports published from 2007 to 2008, with sample sizes ranging from 32 to 279 patients, most participants received the continuous-flow device as a bridge to transplantation. Survival rates at 6 months were between 67% and 87%, and between 50% and 80% at 1 year. These rates were similar to those reported from the INTERMACS registry. An additional report from INTERMACS comparing the HeartMate II with other LVADs for patients who received them as a bridge to transplantation reported that 91% and 80% of HeartMate II and other LVAD patients, respectively, reached transplant, cardiac recovery, or ongoing LVAD support by 6 months. A study by Patel et al compared HeartMate I and HeartMate II recipients at a single center, finding similar rates of 1-year survival and subsequent development of right heart failure. Serious adverse events occurring after HeartMate II implantation include bleeding episodes requiring reoperation, stroke, infection, and device failure.

Effects of Pretransplant VADs on Transplant Outcomes

Published studies continue to report that the use of a VAD does not compromise the success of a subsequent heart transplant and, in fact, may improve posttransplant survival, thus improving the use of
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donor hearts. A systematic review published in 2011 examined the evidence on the effect of VADs on posttransplant outcomes. This review included 31 observational studies that compared transplant outcomes in patients who did and did not have pretransplant VAD. Survival at 1 year was more likely in patients who had VAD treatment, but this benefit was specific to patients who received an intracorporeal device (relative risk [RR], 1.8; 95% confidence interval [CI], 1.53 to 2.13). For patients treated with an extracorporeal device, the likelihood of survival did not differ from patients not treated with a VAD (RR=1.08; 95% confidence interval [CI], 0.95 to 1.22). There was no difference in the risk of rejection between patients who did and did not receive LVAD treatment.

In 2014, Deo et al reported no significant differences in outcomes for 37 patients bridged to transplant with a VAD and 70 patients who underwent a heart transplant directly. Data from the United Network for Organ Sharing (UNOS), reported by Grimm et al (2016), suggested that patients bridged to transplant with an LVAD have better outcomes than those bridged with TAH or biventricular assist devices.

**Pediatric Patients**

There is 1 FDA-approved device, the EXCOR Pediatric VAD, via the humanitarian device exemption (HDE) process, available for use as a bridge to cardiac transplant in children. This HDE approval was based on data from children who were a part of the initial clinical studies of this device. Publications have reported positive outcomes for children using VADs as a bridge to transplantation. Using the United Network for Organ Sharing database, Davies et al reported on use of VADs in pediatric patients undergoing heart transplantation. Their analysis concluded that pediatric patients requiring a pretransplantation VAD have similar long-term survival to those not receiving mechanical circulatory support.

Following FDA approval, Fraser et al evaluated the EXCOR device among 48 children, aged 16 or younger with 2-ventricle circulation who had severe heart failure, despite optimized treatment and were listed for heart transplant. Patients were divided into 2 groups based on body surface area; a historic control group of children receiving circulatory support with ECMO from the Extracorporeal Life Support Organization registry, matched in a 2:1 fashion with study participants based on propensity-score matching. For participants in cohort 1 (body surface area, <0.7 m$^2$), the median survival time had not been reached at 174 days, while in the matched ECMO comparison group, the median survival was 13 days (p<0.001). For participants in cohort 2 (body surface area, 0.7 to <1.5 m$^2$), the median survival was 144 days, compared with 10 days in the matched ECMO group (p<0.001). Rates of adverse events were high in both EXCOR device cohorts, including major bleeding (in 42% and 50% of cohort 1 and cohort 2, respectively), infection (in 63% and 50% of cohort 1 and cohort 2, respectively), and stroke (in 29% of both cohorts).

In 2016, Blume et al published the first analysis of the Pediatric Interagency Registry for Mechanical Circulatory Support (PediMACS), which is a prospective, multicenter registry that collects data on patients who are under age 19 at the time of implant, and includes those implanted with either durable or temporary VADs. At the time of analysis, the registry included 241 patients; of these, 41 were implanted with a temporary device only, leaving 200 patients implanted with VADs for the present study. Most patients (73%) had an underlying diagnosis of cardiomyopathy. At the time of implantation, 64% were listed for transplant, while 29% were implanted with a "bridge to candidacy" strategy. A total of 7% were implanted with a
destination therapy strategy. Actuarial survival at both 6 months and 1 year was 81%. At 6 months, 58% of patients were transplanted.

Also in 2016, Wehman et al reported on posttransplant survival outcomes for pediatric patients who received a VAD, ECMO, or no mechanical circulatory support (MCS), in the pretransplant period. The study included 2777 pediatric patients who underwent heart transplant from 2005 to 2012 who were identified through the UNOS database, of whom 428 were bridged with VADs and 189 were bridged with ECMO. In unadjusted analysis, the actuarial 5-year survival was highest in the direct-to-transplant group (77%), followed by the VAD group (49%) and then the ECMO group (35%). In a proportional hazards model to predict time to death, restricted to the first 4 months posttransplant, ECMO bridging was significantly associated with higher risk of death (adjusted hazard ratio [HR], 2.77 vs direct-to-transplant; 95% CI, 2.12 to 3.61; p<0.001). However, a model to predict time to death excluding deaths in the first 4 months posttransplant, the bridging group was not significantly associated with risk of death.

In 2013, Almond et al reported results from a prospective, multicenter registry to evaluate outcomes in children who received the Berlin Heart EXCOR device as a bridge to transplant. This study included a broader patient population than the Fraser study (discussed above). All patients were followed from the time of EXCOR implantation until transplantation, death, or recovery. The study included 204 children, 67% of whom received the device under compassionate use. Survival at 12 months on EXCOR support was 75%, including 64% who survived to transplantation, 6% who recovered (device explanted and patient survived 30 days), and 5% who were alive with the device in place. In a follow-up study that evaluated 204 children from the same registry, Jordan et al reported relatively high rates of neurologic events in pediatric patients treated with the EXCOR device (29% of patients), typically early in the course of device use.

In 2016, Chen et al reported on a retrospective, single-center series of pediatric patients with continuous-flow VADs, with a focus on outpatient experiences. The series included 17 children implanted with an intracorporeal device from 2010 to 2014. Eight (47%) patients were discharged after a median postimplant hospitalization duration of 49 days. Adverse events were common in outpatients, most frequently major device malfunction (31% [5/16] events) and cardiac arrhythmias (31% [5/16] events). At the time of analysis, 4 patients had received an orthotopic heart transplant, 2 were on ongoing support, and 1 each had been transferred or died.

Another retrospective, single-center series of pediatric patients reported on outcomes with short-term continuous-flow VADs, which including the Thoratec PediMag or CentriMag, or the Maquet RotaFlow. From 2015 to 2014, 27 children were supported with one of these devices, most commonly for congenital heart disease (42%). The median duration of support was 12 days, and 67% of all short-term continuous-flow VAD runs (19 of 28 runs) led to hospital discharge.

Section Summary: VADs as Bridge to Transplant
In adults, the evidence on the efficacy of VADs as bridge to transplant consists of numerous uncontrolled trials and trials comparing different VADs among patients who have no other treatment options. In children, the evidence consists of several uncontrolled trials and 1 trial with historical controls. These studies report that substantial numbers of patients survive to transplant in situations in which survival would not be otherwise expected. Despite the lack of high-quality controlled trials, this evidence is sufficient to determine
Total Artificial Hearts and Implantable Ventricular Assist Devices

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that outcomes are improved in patients who have no other options for survival. The impact of pretransplant LVADs on survival from transplant is uncertain, with some studies reporting worse survival in patients receiving LVADs, but other studies reporting similar or improved survival.

VADs as Destination Therapy
The policy regarding VADs as destination therapy is based on a 2002 TEC Assessment that offered the following observations and conclusions:

- The available evidence comes from a single, well-designed and rigorously conducted randomized trial, known as the REMATCH study. The study was a cooperative effort of Thoratec, Columbia University, and the National Institutes of Health.
- The randomized trial found that patients with end stage heart failure who are not candidates for cardiac transplantation have significantly better survival on a VAD compared with treatment by optimal medical therapy. Median survival was improved by approximately 8.5 months. Serious adverse events were more common in the VAD group, but these appear to be outweighed by this group’s better outcomes on function; New York Heart Association (NYHA) class was significantly improved, as was quality of life among those living to 12 months.
- VAD patients spend a greater relative proportion of time inside the hospital than medical management patients do, but the survival advantage would mean a longer absolute time outside the hospital.

Park et al published an extended 2-year follow-up of patients from the REMATCH trial, which found that survival and quality-of-life benefits were still apparent. In addition, this study and other case series suggested continuing improvement in outcomes related to ongoing improvements in the device and in patient management. However, the durability of the HeartMate device used in the REMATCH trial was a concern (eg, at 1 participating institution, all 6 long-term survivors required device change-outs).

After release of the REMATCH trial results, Rogers et al published results from a prospective, nonrandomized clinical trial comparing LVAD as destination therapy to optimal medical therapy for patients with heart failure who were not candidates for heart transplant. Fifty-five patients who had NYHA functional class IV symptoms and who failed weaning from inotropic support were offered a Novacor LVAD; 18 did not receive a device due to preference or device unavailability and acted as a control group. The LVAD-treated patients had superior survival rates at 6 months (46% vs 22%; p=0.03) and 12 months (27% vs 11%; p=0.02), along with fewer adverse events.

A subsequent prospective observational study comparing LVAD support (n=97) to optimal medical therapy (n=103) for patients with heart failure not requiring inotropes also reported superior survival and health-related quality of life in LVAD-treated patients. Twelve-month survival was 80% in the LVAD group compared with 63% in the best medical therapy group (p=0.022).

In an FDA-required postapproval study of the HeartMate II device for destination therapy, which included the first 247 HeartMate II patients identified as eligible for the device as destination therapy, outcomes and adverse events did not differ significantly from those of the original trial, which compared patients who
received the HeartMate II to earlier generation devices (Slaughter et al [2009], described next). Survival in the postapproval cohort was 82% and 69% at 1 and 2 years postoperatively, respectively.

**Section Summary: VADs as Destination Therapy**
The main piece of evidence on the efficacy of LVADs as destination therapy in patients who are not transplant candidates is from a multicenter randomized controlled trial (RCT), the REMATCH study. This trial reported that the use of LVADs led to improvements in survival, quality of life, and functional status. This evidence is sufficient to establish that health outcomes are improved for this patient population.

**Comparative Efficacy of Continuous Flow Versus Pulsatile Flow Devices**
In December 2009, Slaughter et al published data from an unblinded randomized multicenter trial comparing a continuous flow device with a pulsatile device. Subjects were randomly assigned to continuous-flow or pulsatile-flow devices on a 2:1 block-randomization basis. The primary outcome measured was a composite end point of 2-year survival, free of disabling stroke, or need for device replacement. Continuous flow patients (n=134) reached the primary outcome at a rate of 46% (95% CI, 38 to 55) compared with pulsatile-flow patients’ (n=66) rate of 11% (95% CI, 3 to 18), which was a significant difference (p<0.001). Analysis of constituent factors indicated that a lower rate of devices needing replacement in the continuous flow group had the largest effect on the composite end point; 2-year death rate also favored this device (58% vs 24%, respectively; p=0.008). Stroke and death (within 2 years of implantation) were similar in the 2 groups (stroke rate, 12%; death rate, 36%). Quality-of-life scores were also similar in the 2 groups. Although unblinded, this randomized trial adds to the evidence favoring continuous flow devices.

Nativi et al published a nonrandomized comparison of pulsatile versus continuous flow devices using data from the registry of the International Society for Heart and Lung Transplantation on 8557 patients undergoing transplant. Comparisons were made among patients receiving a pulsatile LVAD, a continuous flow LVAD, and no LVAD. Two time periods were used for analysis; the first was pre-2004, when nearly all LVADs were pulsatile devices, and post-2004 when continuous use devices began to be used in clinical care. Comparing the first time period with the second time period, there was a significantly greater risk of mortality in the first time period compared with the second time period (RR=1.30; 95% CI, 1.03 to 1.65; p=0.03). When analysis was confined to the second time period, there was no significant improvement in survival for the continuous group compared with the pulsatile group (RR=1.25; 95% CI, 1.03 to 1.65; p=0.03).

Dell’Aquila et al compared outcomes for patients treated with a third-generation continuous flow device, the HeartWare device, with those for patients treated with earlier generation devices in a single-center study. Comparison group patients received either an earlier generation continuous flow device or a pulsatile flow device. Of 287 patients who received VAD support from 1993 to 2012, 52 received a HeartWare device, 76 an earlier generation continuous flow device, and 159 a pulsatile device. Survival was significantly better for patients who received a third-generation device, with 24 month survival of 70.4%, compared with 33.7% for patients who received an earlier-generation continuous flow device and 33.8% for patients who received a pulsatile flow device (p=0.013). The difference in survival associated with third-generation devices was more pronounced for higher scores on the INTERMACs scale.
Other nonrandomized studies that have compared outcomes from different types of LVADs have been smaller and/or focused on physiologic outcomes. In some of these studies, the continuous flow devices exhibit greater improvement in physiologic measures, but none of these studies have reported significant differences between devices in clinical outcomes.

**Section Summary: Comparative Efficacy of Continuous-Flow Versus Pulsatile-Flow Devices**

The evidence on the comparative efficacy of different devices consists of 1 RCT and several nonrandomized comparative studies. The RCT reported fairly large differences in a composite outcome measure favoring the continuous flow devices, with increases in revision and reoperation rates for the pulsatile device group being the largest factor driving the difference in outcomes. Other nonrandomized comparative studies, including 1 database study with large numbers of patients, have not reported important differences between devices on clinical outcomes.

**Total Artificial Hearts**

**TAH as Bridge to Transplant**

FDA approval of the CardioWest TAH was based on the results of a nonrandomized, prospective study of 81 patients. Patients had failed inotropic therapy and had biventricular failure and thus were not considered appropriate candidates for an LVAD. The rate of survival to transplant was 79%, which was considered comparable with the experience with LVAD in patients with LV failure. The mean time from entry into the study until transplantation or death was 79.1 days.

Other case series have been reported on outcomes of the TAH as a bridge to transplant. For example, Copeland et al reported on 101 patients treated with the SynCardia artificial heart as a bridge to transplant. All patients either met established criteria for mechanically assisted circulatory support, or were failing medical therapy on multiple inotropic drugs. The mean support time was 87 days, with a range of 1 to 441 days. Survival to transplant was 68.3% (69/101). Of the 32 deaths before transplant, 13 were due to multiple organ failure, 6 were due to pulmonary failure, and 4 were due to neurologic injury. Survival after transplant at 1, 5, and 10 years, respectively, was 76.8%, 60.5%, and 41.2%.

**TAH as Destination Therapy**

Data concerning the artificial heart are available from information concerning FDA approval and from a published article describing results for the first 7 patients. FDA indicated that their decision was based on the company's laboratory and animal testing and on a small clinical study of 14 patients that was conducted by Abiomed. The patients had a 1-month survival prognosis of not more than 30%, were not eligible for cardiac transplants, and were felt to not benefit from VAD therapy. The study was reported to show that the device is safe and has likely benefit for people with severe heart failure whose death is imminent and for whom no alternative treatments are available. Of the 14 patients in the study, 12 survived surgery. Mean duration of support for the patients was 5.3 months. In some cases, the device extended survival by several months; survival was 17 months in 1 patient. Six patients were ambulatory; 1 patient was discharged home. Complications included postoperative bleeding and neurologic events. Device-related infection was "non-existent."
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Longer Term Follow-Up
Torregrossa et al reported on 47 patients who received a TAH at 10 worldwide centers and had the device implanted for more than 1 year. Patients were implanted for dilated cardiomyopathy (n=23), ischemic cardiomyopathy (n=15), and “other” reasons (n=9). Over a median support time of 554 days (range, 365-1373 days), 34 patients (72%) were successfully transplanted, 12 patients (24%) died while on device support, and 1 patient (2%) was still supported. Device failure occurred in 5 patients (10%). Major complications were common, including systemic infection in 25 patients (53%), driveline infections in 13 patients (27%), thromboembolic events in 9 patients (19%), and hemorrhagic events in 7 patients (14%). Two of the deaths occurred secondary to device failure.

Section Summary: Total Artificial Hearts
There is a smaller amount of evidence on the use of TAH as a bridge to transplantation, or as destination therapy, compared with the use of LVADs. The type of evidence on bridge to transplant is similar to that for LVADs (ie, case series reporting substantial survival rates in patients without other alternatives). Therefore, this evidence is sufficient to conclude that TAH improves outcomes for these patients similar to LVADs and is a reasonable alternative for patients who require bridge to transplantation but who are ineligible for other types of support devices. Although TAHs show promise for use as destination therapy in patients who have no other treatment options, the available data on their use is extremely limited. There is insufficient evidence on the use of TAH as destination therapy to support conclusions about the efficacy of TAH in this setting.

Percutaneous Ventricular Assist Devices
pVADs as an Alternative to Intra-Aortic Balloon Pump in Cardiogenic Shock
Romeo et al (2016) reported on a systematic review and meta-analysis that evaluated a variety of percutaneous mechanical support methods, including pVADs, for patients with cardiogenic shock due to AMI who were undergoing revascularization. This review included the 3 RCTs (described above) comparing pVADs with intra-aortic balloon pumps (IABPs), along with 3 observational studies. In the comparison of pVADs with IABP, the reviewers found that in-hospital mortality (the primary outcome of the analysis) was nonsignificantly increased in the pVAD group.

Three RCTs have been published that compare pVADs with IABPs for patients with cardiogenic shock, along with a systematic review and meta-analysis of these 3 trials. The meta-analysis was published in 2009 by Cheng et al. The 3 RCTs enrolled a total of 100 patients, 53 treated with a pVAD and 47 treated with an IABP. All 3 study populations included patients with acute myocardial infarction (MI) and cardiovascular shock; 1 of the trials restricted this population to patients who were postrevascularization in the acute MI setting. The primary outcomes reported were 30-day mortality, hemodynamic measures of LV pump function, and adverse events.

None of the three trials reported an improvement in mortality associated with pVAD use. The combined analysis estimated the relative risk for death in pVAD patients as 1.06 (95% CI, 0.68 to 1.66; p=0.80). All three trials reported an improvement in LV hemodynamics in the pVAD group. On combined analysis, there was a mean increase in cardiac index of 0.35 L/min/m² for the pVAD group, an increase in mean arterial pressure of 12.8 mm Hg (95% CI, 3.6 to 22.0; p<0.001), and a decrease in pulmonary capillary wedge pressure.
pressure of 5.3 mm Hg (95% CI, 1.2 to 9.4; p<0.05). Complications were more common in the pVAD group. On combined analysis, patients in the pVAD group had a significantly increased likelihood of bleeding events with a relative risk of 2.35 (95% CI, 1.40 to 3.93). Leg ischemia was also more common in the pVAD group, but this difference did not meet statistical significance (RR=2.59; 95% CI, 0.75 to 8.97; p=0.13).

O'Neill et al compared outcomes for patients with acute MI complicated by cardiogenic shock who received pVAD support pre–percutaneous coronary intervention (PCI) with those who received pVAD support post-PCI using data from 154 consecutive patients enrolled in a multicenter registry. Patients who received pVAD support pre-PCI had higher survival to discharge compared with those who received pVAD support post-PCI (65.1% vs 40.7%; p=0.003). In multivariable analysis, receiving pVAD support pre-PCI was associated with in-hospital survival (odds ratio [OR], 0.37; 95% CI, 0.17 to 0.79; p=0.01). However, the potential for underlying differences in patient groups other than the use of pVAD support makes the study's implications uncertain.

Case series of patients treated with pVADs as an alternative to IABP in cardiogenic shock have been published and report high success rates as a bridge to alternative therapies. However, given the availability of RCT evidence, these studies add a limited amount to the body of evidence on the efficacy of pVADs for the management of cardiogenic shock.

**pVADs as Bridge to Recovery in Cardiogenic Shock Refractory to IABP**

Case series of patients with cardiogenic shock refractory to IABP who were treated with pVAD have also been published. In the largest series, Kar et al treated 117 patients who had severe, refractory cardiogenic shock with the TandemHeart System. Eighty patients had ischemic cardiomyopathy, and 37 had nonischemic cardiomyopathy. There were significant improvements in all hemodynamic measures following LVAD placement. For example, cardiac index increased from 0.52±0.8 L/min/m² to 3.0±0.9 L/min/m² (p<0.001), and systolic blood pressure increased from 75±15 mm Hg to 100±15 mm Hg (p<0.001). Complications were common post-LVAD implantation. Thirty-four patients had bleeding around the cannula site (29.1%), and 35 developed sepsis during the hospitalization (29.9%). Groin hematoma occurred in 6 patients (5.1%); limb ischemia in 4 patients (3.4%); femoral artery dissection or perforation in 2 patients (1.7%); stroke in 8 patients (6.8%); coagulopathy in 13 patients (11.0%).

**pVADs as Ancillary Support in High-Risk Patients Undergoing High-Risk Cardiac Procedures**

In 2016, Briasoulis et al reported on a meta-analysis of pVAD devices as an adjunct to high-risk PCI. The reviewers included RCTs and cohort studies, identifying 18 nonrandomized observational studies and 1 RCT. The single RCT identified was the PROTECT II trial described in more detail below. In the observational studies, the sample sizes ranged from 7 to 637 patients. In pooled analysis, the 30-day mortality rate following Impella-assisted high-risk PCI was 3.5% (95% CI, 2.2% to 4.8%; I²=20%), while that for TandemHeart-assisted high-risk PCI was 8% (95% CI, 2.9% to 13.1%; I²=55%). The pooled vascular complication rates were 4.9% (95% CI, 2.3% to 7.6%) and 6.5% (95% CI, 3.2% to 9.9%) for the Impella and the TandemHeart, respectively.

The PROTECT trial evaluated whether the Impella 2.5 system improves outcomes for patients undergoing high-risk PCI procedures. PROTECT I was a feasibility study of 20 patients who had left main disease or...
last patent coronary conduit that required revascularization but who were not candidates for coronary artery bypass graft surgery. High-risk PCI was performed using the Impella system for circulatory support. All procedures were successfully completed without any hemodynamic compromise in procedure. Two (10%) patient died within 30 days and 2 (10%) patients had a periprocedural MI. Two other patients had evidence of hemolysis, which was transient and resolved without sequelae.

The PROTECT II trial was planned as an RCT to compare the Impella system with IABP in patients undergoing high-risk PCI procedures. Enrollment was planned for 654 patients from 50 clinical centers. The primary end point was the composite of 10 different complications occurring within 30 days of the procedure, with the authors hypothesizing a 10% absolute decrease in the complication rate for patients in the pVAD group. The trial was discontinued prematurely in late 2010 due to futility, after an interim analysis of the first 327 patients enrolled revealed that the primary end point could not be reached. When stopped, 452 patients had been enrolled, 3 of whom withdrew consent and 1 who died. Results were published by O’Neill et al in 2012. The study’s primary analysis was intention to treat and included all 448 patients randomly assigned to the Impella system (n=225) or IABP (n=223). The primary composite end point of major adverse effects at 30 days occurred in 35.1% of Impella patients and in 40.1% of the IABP patients (p=0.277). There was no significant difference in the occurrence of in-hospital death, stroke, or MI between the Impella patients and the IABP patients.

In a prespecified subgroup analysis of the PROTECT II trial, Kovacic et al compared outcomes for the Impella system and IABP among 325 patients with 3-vessel disease with a LVEF of less than or equal to 30%. In the 3-vessel disease subgroup, 167 subjects were randomized to PCI with Impella support and 158 to PCI with IABP support. PCI characteristics differed in that rotational atherectomy was more aggressively used in the Impella-support group, with more passes per patient (5.6 vs 2.8, p=0.002) and more passes per coronary lesion (3.4 vs 1.7, p=0.001). Acute procedural revascularization results did not differ between groups. At 30 days, the major adverse event rate did not differ significantly between groups (32.9% of Impella patients vs 42.4% of IABP patients, p=0.078). At 90 days, Impella patients (39.5%) had a significantly lower major adverse event rate compared with IABP patients (51.0%; p=0.039). The 90-day event rates for the individual components of the composite major adverse event score differed only for severe hypotension requiring treatment, which was more common in patients treated with IABP (7.6% vs 2.4%, p=0.029).

In a post hoc analysis, results of the PROTECT II trial were reanalyzed by Dangas et al, using a revised definition of MI in the determination of patients with major adverse events and major adverse cardiac and cerebral events. Unlike the original trial, which used a cutoff of 3 times the upper limit of normal for biomarker elevation to define periprocedural MI, the authors used a cutoff of 8 times the upper limit of normal for biomarker elevation or the presence of Q waves to define periprocedural MI. In multivariable analysis, compared with IABP, treatment with the Impella system was associated with freedom from 90-day major adverse events (OR=0.75; 95% CI, 0.61 to 0.92; p=0.007) and major adverse cardiac and cerebral events (OR=0.76; 95% CI, 0.61 to 0.96; p=0.020).

Other case series have described pVAD use in high-risk patients undergoing an invasive cardiac procedure. Sjauw et al retrospectively analyzed 144 consecutive patients undergoing high-risk PCI with pVAD support.
(Impella system) from a European registry. End points included successful device function and incidence of adverse events at 30 days. The device was successfully implanted in all 144 patients. There was 1 periprocedural death and 8 deaths at 30 days for a mortality rate of 5.5%. Bleeding requiring transfusion or surgery occurred in 6.2% of patients, and vascular access site complications occurred in 4.0%. There was 1 (0.7%) stroke, and no MIs were reported. Maini et al performed a similar retrospective analysis of 175 patients undergoing high-risk PCI with pVAD support with the Impella 2.5 circulatory support system. The primary safety end point was the incidence of major adverse cardiac events at 30 days. Secondary end points included device safety and efficacy and patient outcomes at 30 days and 12 months. Angiographic revascularization was successful in 99% of patients. At 30-day follow-up, the major adverse cardiac event rate was 8%; survival was 96%, 91%, and 88% at 30 days, 6 months, and 12 months, respectively. Secondary safety end points occurring most frequently included acute renal dysfunction (2.8%), hypotension on support (3.4%), ventricular tachycardia (VT), or cardiopulmonary resuscitation (2.8%); other vascular complications included vessel dissection and arteriovenous fistula (3.4%), hematomas ipsi- or contralateral to the device insertion site (8.6%), infection (5.1%), and blood transfusion (9.7%).

Reddy et al reported outcomes for a series of 66 patients enrolled in a prospective, multicenter registry who underwent VT ablation with a pVAD or IABP. Twenty-two patients underwent ablation with IABP assistance, while 44 underwent ablation with either the TandemHeart or Impella pVAD device (non-IABP group). Compared with patients who received support with an IABP, those who received support with a pVAD had more unstable VTs that could be mapped and ablated (1.05 vs 0.32, p<0.001), more VTs that could be terminated by ablation (1.59 vs 0.91, p=0.001), and fewer VTs terminated with rescue shocks (1.9 vs 3.0, p=0.049). More pVAD-supported patients could undergo entrainment/activation mapping (82% vs 59%, p=0.046). Mortality and VT recurrence did not differ over the study follow-up period (average, 12 months).

In a retrospective study, Aryana et al reported procedural and clinical outcomes for 68 consecutive unstable patients with scar-mediated epicardial or endocardial VT who underwent ablation with or without pVAD support. Thirty-four patients had hemodynamic support periprocedurally with a pVAD. pVAD- and non-pVAD-supported patients were similar at baseline, with no differences in procedural success rates between groups. Compared with non-pVAD-supported patients, patients in the pVAD group had a longer maximum time in unstable VT (27.4 min vs 5.3 min, p<0.001), more VT ablations per procedure (1.2 vs 0.4, p<0.001), a shorter radiofrequency ablation time (53 seconds vs 68 seconds, p=0.022), and a shorter hospital length of stay (4.1 days vs 5.4 days, p=0.013). Over a follow-up period of 19 months, rates of VT recurrence did not differ between groups.

**Section Summary: Percutaneous Ventricular Assist Devices**

pVADs have been tested in RCTs and uncontrolled studies of patients with cardiogenic shock and in patients undergoing high-risk cardiac interventions. The RCTs have not consistently reported a benefit for use of pVADs. In addition, the RCTs and case series have reported high rates of adverse events that may outweigh any potential benefits. As a result, the evidence on pVADs does not demonstrate that pVADs are associated with improvements in health outcomes for patients with cardiogenic shock or for patients undergoing high-risk cardiac interventions.
Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 2.

Table 2. Summary of Key Trials

<table>
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<th>NCT No.</th>
<th>Trial Name</th>
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<th>Completion Date</th>
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NCT: national clinical trial.
a Denotes industry-sponsored or cosponsored trial.

Summary of Evidence
For individuals who have end-stage heart failure who receive a VAD as bridge to transplant, the evidence includes single-arm clinical trials and observational studies. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, and treatment-related mortality and morbidity. There is a substantial body of evidence from clinical trials and observational studies supporting implantable VADs as a bridge to transplant in patients with end-stage heart failure, possibly improving mortality, as well as quality of life. These studies have reported that substantial numbers of patients have survived to transplant in situations in which survival would not be otherwise expected. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals who have end-stage heart failure who receive a VAD as destination therapy, the evidence includes 1 clinical trial and multiple single-arm studies. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, and treatment-related mortality and morbidity. A well-designed clinical trial, with 2 years of follow-up data, have demonstrated an advantage of implantable VADs as destination therapy for patients ineligible for heart transplant. Despite an increase in adverse events, both mortality and quality of life appear to be improved for these patients. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals who have end-stage heart failure who receive a TAH as bridge to transplant, the evidence includes case series. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, and treatment-related mortality and morbidity. Compared with VADs, the evidence for TAHs in these
settings is less robust. However, the lack of medical or surgical options for these patients and what evidence case series provide, TAH is likely to improve outcomes for a carefully selected population with end stage biventricular heart failure awaiting transplant who are not appropriate candidates for a left ventricular assist device. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals who have end-stage heart failure who receive a TAH as destination therapy, the evidence includes 2 case series. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, and treatment-related mortality and morbidity. The body of evidence for TAHs as destination therapy is very limited. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with cardiogenic shock or who undergo a high-risk cardiac procedures who receive a pVAD, the evidence includes RCTs. Relevant outcomes are overall survival, symptoms, morbid events, functional outcomes, quality of life, and treatment-related mortality and morbidity. Three RCTs of pVAD versus intra-aortic balloon pump (IABP) for patients in cardiogenic shock failed to demonstrate a mortality benefit and reported higher complications associated with pVAD use. A fourth RCT comparing pVAD with IABP as an adjunct to high-risk percutaneous coronary interventions was terminated early due to futility; analysis of enrolled subjects did not demonstrate significant improvements in the pVAD group. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with cardiogenic shock refractory to IABP who receive a pVAD, the evidence includes case series. Relevant outcomes are overall survival, symptoms, morbid events, functional outcomes, quality of life, and treatment-related mortality and morbidity. Case series of patients with cardiogenic shock refractory to IABP have reported improved hemodynamic parameters following pVAD placement. However, these uncontrolled series does not provide evidence that pVADs improve mortality, and high rates of complications have been reported with pVAD use. The evidence is insufficient to determine the effects of the technology on health outcomes.

References
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Total Artificial Hearts and Implantable Ventricular Assist Devices

Policy # 00246
Original Effective Date: 01/20/2010
Current Effective Date: 11/16/2016


34. Blue Cross and Blue Shield Association. Technology Evaluation Center (TEC). Left ventricular assist devices as destination therapy for end-stage heart failure. TEC Assessments 2002. Volume 17, Tab 19. PMID


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01/07/2010  Medical Policy Committee approval
01/20/2010  Medical Policy Implementation Committee approval. New policy.
01/06/2011  Medical Policy Committee approval
01/19/2011  Medical Policy Implementation Committee approval. Title changed. Policy statements revised to address only implantable VADs and total artificial hearts.
04/12/2012  Medical Policy Committee approval
04/25/2012  Medical Policy Implementation Committee approval. Percutaneous VADs added to policy investigational statement and rationale.
04/04/2013  Medical Policy Committee review

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85. McMurray JJ, Adamopoulos S, Anker SD, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur Heart J. Jul 2012;33(14):1787-1847. PMID 22611136

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04/24/2013  Medical Policy Implementation Committee approval. Added “Implantable” to the beginning of the 2nd coverage statement under Bridge to Transplant to make it consistent with the other coverage statements and the focus of the policy. Coverage statement on children amended; age range changed from 5-16 to 0-16, reflecting the approval of the BERLIN heart EXCOR device for pediatric patients aged 0-16. Clause added to coverage statement on total artificial hearts that says “…or are undergoing evaluation to determine candidacy for heart transplantation…”.

08/07/2014  Medical Policy Committee review
08/20/2014  Medical Policy Implementation Committee approval. Coverage statement unchanged.
08/03/2015  Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
10/29/2015  Medical Policy Committee review
11/03/2016  Medical Policy Committee review
11/16/2016  Medical Policy Implementation Committee approval. No change to coverage.
01/01/2017  Coding update: Removing ICD-9 Diagnosis Codes and CPT coding update

Next Scheduled Review Date:  11/2017

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®), copyright 2015 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

<table>
<thead>
<tr>
<th>Code Type</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>0051T, 0052T, 0053T, 33975, 33976, 33977, 33978, 33979, 33980, 33981, 33982, 33983, 33990, 33991, 33992, 33993, 93750 New codes eff 1/1/17: 0451T, 0452T, 0453T, 0454T, 0455T, 0456T, 0457T, 0458T, 0459T, 0460T, 0461T, 0462T, 0463T</td>
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<tr>
<td>HPCPCS</td>
<td>Q0478, Q0479, Q0480, Q0481, Q0482, Q0483, Q0484, Q0485, Q0486, Q0487, Q0488, Q0489, Q0490, Q0491, Q0492, Q0493, Q0494, Q0495, Q0496, Q0497, Q0498, Q0499, Q0500, Q0501, Q0502, Q0503, Q0504, Q0506, Q0507, Q0508, Q0509</td>
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<tr>
<td>ICD-10 Diagnosis</td>
<td>I09.81, I11.0, I13.0, I13.2, I50.20-I50.23, I50.30-I50.33, I50.40-I50.43, I50.9</td>
</tr>
</tbody>
</table>
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*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
   1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
   2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
   3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;

B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and

C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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