Medical Coverage Policy

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Ventricular Assist Devices (VADs), Percutaneous Cardiac Support Systems and Total Artificial Heart

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Related Coverage Resources

External Counterpulsation
Heart, Lung, and Heart-Lung Transplantation

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s).

Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This Coverage Policy addresses mechanical circulatory assist devices which include the ventricular assist devices (VADs), percutaneous ventricular assist devices (pVADs), permanently implantable aortic counterpulsation VADs and total artificial heart (TAH).

Coverage Policy

Implantable Ventricular Assist Devices (VADs)

A U.S. Food and Drug Administration (FDA)-approved VAD is considered medically necessary when used in accordance with device-specific, FDA-approved indications and contraindications when ANY of the following criteria is met:

- Individual in acute cardiogenic shock when recovery is expected
- Individual unable to be weaned from cardiopulmonary bypass following cardiac surgery when recovery is expected
- Individual in whom heart transplantation is anticipated and who is otherwise not expected to survive until transplantation
- Individual not expected to be considered a candidate for heart transplantation, when ALL of the following criteria are met
  - New York Heart Association (NYHA) Class IV end-stage left ventricular heart failure
  - left ventricular ejection fraction (LVEF) < 25%
  - demonstrated functional limitations, with a peak oxygen consumption of ≤14 milliliters per kilogram of body weight per minute
  - failure to respond to optimal medical therapy for 45 of the last 60 days, or dependence on intra-aortic balloon pump for a period of seven days, or inotropes for a period of at least fourteen days

The CentriMag® Blood Pump is considered medically necessary for EITHER of the following:

- use as a right ventricular assist device (RVAD) for temporary circulatory support in accordance with the FDA's Humanitarian Device Exemption (HDE) requirements when BOTH of the following criteria are met:
  - device is used for up to thirty days for an individual in cardiogenic shock due to acute right ventricular failure
  - individual is willing and able to be treated with heparin or an appropriate alternative anticoagulation

- use for up to six hours to provide hemodynamic stabilization in an individual in need of cardiopulmonary support

The HeartAssist 5® Pediatric VAD is considered medically necessary as a bridge to cardiac transplantation in a child when ALL of the following criteria are met, in accordance with the FDA's Humanitarian Device Exemption (HDE) requirements:

- age 5–16
- body surface area (BSA) ≥ 0.7 m^2 and < 1.5 m^2
- in NYHA Class IV end-stage (i.e., left ventriculasur) heart failure refractory to medical therapy
- listed candidate for cardiac transplantation
- none of the following contraindications:
  - primary coagulopathy or platelet disorders
  - anatomical anomalies that would prevent surgical connection of the outflow graft to the ascending aorta
  - right ventricular failure unresolved by medical therapy

The Berlin Heart EXCOR® Pediatric Ventricular Assist Device is considered medically necessary as a bridge to cardiac transplantation in a child with severe isolated left ventricular or biventricular dysfunction who is a candidate for cardiac transplant and requires circulatory support, in accordance with the FDA's requirements.

A VAD in an individual with ANY of the following contraindications to permanent (implantable) placement is considered not medically necessary (this list may not be all-inclusive):

- persistent, recurrent or unsuccessfully-treated major or systemic infections
- systemic illness or comorbidities that would be expected to substantially negatively impact the successful completion and/or outcome of device placement
- lack of sufficient care-giver support

<u>Percutaneous Ventricular Assist Devices (VADs)</u>

The TandemHeart® PTVA® System, the Impella 2.5®, Impella 5.0®, Impella 5.5® with SmartAssist®, or Impella CP®, and Impella CP® with SmartAssist® are considered medically necessary for the treatment of cardiogenic shock.

Additionally, the Impella 2.5, Impella CP®, and Impella CP® with SmartAssist Systems® are considered medically necessary for use during high-risk percutaneous coronary interventions (PCI) for EITHER of the following:

- PCI on an unprotected left main or last patent coronary vessel with left ventricular ejection fraction (LVEF) ≤ 35%.
- PCI for three-vessel disease with LVEF ≤ 30%.

The Impella RP System is considered medically necessary for up to 14 days in a child or adult with a BSA ≥ 1.5m^2 for the treatment of acute right heart failure or decompensation following left ventricular assist device implantation, myocardial infarction, heart transplant, or open-heart surgery.

A percutaneous ventricular assist device for any other indication considered not medically necessary.

<u>Implantable Aortic Counterpulsation Ventricular Assist Devices (VADs)</u>

A permanently implantable aortic counterpulsation VAD for any indication is considered experimental, investigational or unproven.

Total Artificial Heart

The SynCardia temporary Total Artificial Heart (SynCardia Systems, Inc., Tucson, AZ) is considered medically necessary as a bridge to transplantation in an individual who is transplant-eligible and at risk of imminent death from biventricular failure.

The SynCardia Freedom® Driver System is considered medically necessary in an individual who is clinically stable and discharge is planned following medically necessary implantation of the SynCardia temporary Total Artificial Heart.

The SynCardia temporary Total Artificial Heart or SynCardia Freedom Driver System is considered not medically necessary for any other indication.

Health Equity Considerations

Health equity is the highest level of health for all people; health inequity is the avoidable difference in health status or distribution of health resources due to the social conditions in which people are born, grow, live, work, and age.

Social determinants of health are the conditions in the environment that affect a wide range of health, functioning, and quality of life outcomes and risks. Examples include safe housing, transportation, and neighborhoods; racism, discrimination and violence; education, job opportunities and income; access to nutritious foods and physical activity opportunities; access to clean air and water; and language and literacy skills.

According to a scientific statement from the American Heart Association on social determinants of health (SDOH) in the care of patients with heart failure (HF), there are an estimated 550,000 new cases of HF diagnosed each year accounting for more than 1.9 hospitalizations and $31 billion annually nationwide. The statement identifies several downstream SDOH compounding the complexity of HF management including: socioeconomic position; access to care; environment; race, ethnicity, sex, age, and sexual minorities; social support; and health literacy. The authors found that compared to whites, Blacks have an increased prevalence of HF and disproportionately poor outcomes. This disparity was found to be attributed to, in part, a higher prevalence of risk factors such as uncontrolled hypertension, endothelial dysfunction, and deleterious genetic polymorphisms among nonwhites. Additionally, prior to age 50, Blacks have a higher incidence of HF compared to whites. It is thought that this is due to a higher prevalence of hypertension, diabetes mellitus, and low socioeconomic status. Women tend to experience symptoms of HF that differ from men and despite making up 50% of the American population diagnosed with HF, women are underrepresented in trials evaluating HF therapy. The statement points to several interventions to address these disparities including: "developing a better understanding of the potential impact of SDOH on HF care; integrating the assessment and data collection related to SDOH for patients with HF into routine care, similar to other cardiac risk factors; designing and implementing interprofessional care teams that maximize patient access to varied perspectives and skill sets, which will facilitate self-care and navigation across the healthcare system; and increasing research examining the SDOH profile of patients with HF and the interventions that can be most beneficial in improving the health outcomes of patients with HF" (White-Williams, et al., 2020).

General Background

Implantable Ventricular Assist Devices:

Ventricular assist devices (VADs), also known as mechanical circulatory support (MCS) devices, function to reduce myocardial work by reducing ventricular preload while maintaining systemic circulation. VADs may be extracorporeal, paracorporeal, implantable with percutaneous power support, or fully implantable, and may provide continuous or pulsatile flow. VADs may be employed on a short-term or long-term basis, or as permanent (destination) therapy. VADs may provide left ventricular support (LVAD), right ventricular support (RVAD), or biventricular support (BiVAD).

Short-term VAD use may provide a bridge to recovery for patients in postcardiotomy shock or those with a potentially reversible condition (e.g., acute myocarditis). VADs are also used as a bridge to transplant for patients with heart failure. Heart failure is a complex syndrome that occurs secondary to inherited or acquired abnormalities of cardiac structure and/or function that impair the ability of the left ventricle to eject blood. More than 6.5 million people in the United States live with heart failure, and the incidence of heart failure continues to increase, due in part to the expanded aging population and advances in therapeutic management of cardiovascular disease. Transplantation has become the standard treatment for eligible patients with irreversible severe biventricular failure unresponsive to medical or surgical treatment. The supply of donor hearts has decreased in recent years while the demand has increased. 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. Timely VAD use may restore hemodynamic stability and end-organ function and allow nutritional support and rehabilitation prior to transplantation (White-Williams, et al., 2020; Aaronson, 2019; Hunt, et al., 2009).

Throughout the 1990s, VADs underwent many modifications to improve reliability and reduce complications, as well as to improve utility and ease of use for patients living with these devices. Their improved reliability and mobility has resulted in the use of VADs as destination therapy for selected patients who are not candidates for cardiac transplant. Although VADs are associated with significant risks and complications, they are responsible for improved pre- and post-transplant survival rates and improved quality of life.

Contraindications to Implantable VADs
The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support (MCS) address the issue of patient selection for permanent pump implantation. Candidate selection is one of the most important determinants of successful operative and long-term outcomes for patients receiving implantable MCS. Several factors must be considered during the patient assessment for an MCS device beyond the presence of advanced heart failure. Comorbidities, surgical risk, expectation of benefit, psychological and social support, and the type of device must also be determined prior to implant. Many patients also require a period of aggressive pre-operative medical therapy to optimize their condition prior to MCS (Feldman, et al., 2013). Absolute contraindications to receiving a permanent implantable VAD include irreversible hepatic, renal, or neurological disease, medical nonadherence, and severe psychosocial limitations. Relative contraindications include: age >80 years for destination therapy, obesity or malnutrition, musculoskeletal disease that impairs rehabilitation, active systemic infection or prolonged intubation, untreated malignancy, severe peripheral vascular disease, active substance abuse, unmanaged psychiatric disorder, and lack of social support (Cook, et al., 2017).

U.S. Food and Drug Administration (FDA)

The VADs described below have been granted FDA approval through the premarket approval (PMA), 510(k), or Humanitarian Device Exemption (HDE) process. Device selection is made based on specific FDA-labeled indications.

HeartWare® Ventricular Assist System (VAS) (Medtronic, Inc., Moundsville, MN originally marketed by (HeartWare, Inc., Miami Lakes, FL): The HeartWare VAS originally received FDA approval through the PMA process on November 20, 2012 (P100047) for use as a bridge to cardiac transplantation (BTT) in patients who are at risk of death from refractory end-stage left ventricular heart failure, and is designed for in-hospital and out-of-hospital settings. The HeartWare VAS is a continuous flow blood pump which utilizes magnetic and hydrodynamic forces to elevate and rotate the impeller. The device has received several PMA supplement approvals over the years. On July 26, 2018, the device was approved "for hemodynamic support in patients with advanced, refractory left ventricular heart failure; either as a BTT, myocardial recovery, or as destination therapy (DT) in patients for whom subsequent transplantation is not planned (P100047/S115)."

On February 26th, 2021, the FDA issued a Class I recall (may cause serious injury or death) for the HeartWare system due to safety issues with the carrying cases, driveline cover orientation, and controller power-up sequence. To address these safety issues, the following updates to the instructions for use (IFU) and/or patient manual (PM) were made:

- The IFU was updated to add a lifespan for the carrying cases. If the case is dropped due to a malfunction in the carrying case, it can disconnect the driveline and then interrupt power.
- The PM was updated to instruct patients to keep the driveline cover on while disconnecting or reconnecting the driveline during a controller exchange. This will prevent the driveline locking mechanism from being in the unlocked position which could cause driveline disconnects.
- The IFU and PM will be updated to clarify that the alarm indicator and two battery LEDs will turn red for 2.5 seconds during power-up. This will avoid a potential misinterpretation of the indicator lights as a "red alarm" which could potentiall lead to an unnecessary controller exchange.

The following voluntary recalls have been issued by Medtronic for the HeartWare® VAS since June 2021 (FDA, 2023):

Date	Description
September 2023	Medtronic issued an Urgent Medical Device Communication to notify health care providers that the incompatibility of the Autologs web portal and certain Model 1521 monitors is now resolved. Medtronic first notified health care providers of this issue in May 2023.
August 2023	Medtronic issued an Urgent Medical Device Communication to inform healthcare providers about a newly identified subset of pumps that have a higher risk of failure to restart. This subset is referred to as "subgroup 3". Medtronic provided a list of pump serial numbers that are included in this subset and provided updated patient management recommendations that apply to all three subsets of pumps that have higher failure to restart rates than the general population of pumps. These recommendations include advising patients in these subgroups to contact their VAD coordinator before conducting a controller exchange and providing recommendations to clinicians when considering the need for a controller exchange. Medtronic also provided a summary of clinical experience with the unapproved controller software and details regarding the cumulative failure rates for each device population.

Date	Description
May 2023	Medtronic issued an Urgent Medical Device Communication to inform health care providers of an issue with the HVAD System Autologs web portal. Medtronic's communication explained that logfiles downloaded from the recently updated Model 1521 monitors (Serial Numbers: MON5xxxxxx for U.S. and MON4xxxxxx for Outside of the U.S.) are unable to be processed by the Autologs web portal. There is no impact to the monitor's functionality, ability to download the logfiles to the USB flash drive, display system performance, or adjust controller parameters. If you have issues with the Autologs web portal, contact your Medtronic field representative.
January 2023	Medtronic issued an Urgent Medical Device Correction to request that health care providers and patients return 12 batteries with serial numbers listed in the letter due to battery tab welding defects. These batteries have electronic properties that may be indicative of a welding defect and Medtronic is requesting the return of these batteries to conduct further engineering analysis. The battery tab weld issue is the same issue that is described in the May 2022External Link Disclaimer and June 2022External Link Disclaimer communications.
November 2022	Medtronic issued an Urgent Medical Device Correction to inform health care providers that the driveline boot cover can become stiff over time. If the boot cover hardens, it can be difficult to disconnect the driveline from the controller. Medtronic is providing patient management recommendations, to include inspecting the boot cover routinely. Medtronic advises that hardened boot covers be reported to them so the need to perform a field service procedure to remove the cover can be discussed.
October 2022	Medtronic issued an Urgent Medical Device Correction to inform health care providers that a controller with modified software is available for all requesting hospitals as a back-up if the pump has stopped and the primary controller is unable to restart the pump. The pump failure to restart issue is the same issue that is described in the December 2021 communication, and the modified software is the same that is described in the June 2022 communication.
August 2022	Medtronic issued an Urgent Medical Device Correction to inform health care providers that they will begin exchanging HVAD power sources (batteries, AC and DC adapters) and Monitor data cables with new components that are intended to reduce the risk of damage on the Controller port metal pins. Medtronic previously communicated to health care providers about Controller port bent pins in February 2021. Medtronic is also informing health care providers that the device labeling has been updated with information on useful life and inspection of HVAD System components.
July 2022	Medtronic issued an Urgent Medical Device Correction to provide an update on their investigation into the pump weld defect issue, which was first communicated to health care providers in April 2022. Medtronic's investigation was not able to identify a specific subset of pumps affected by this issue. Medtronic has also confirmed an additional complaint related to this issue.
June 2022	Medtronic issued an Urgent Medical Device Correction to inform health care providers and patients about two issues with the HVAD Battery. • In May 2022, Medtronic recalled a single lot of batteries due to a welding defect affecting internal battery components. Medtronic is now informing all health care providers and patients about this welding defect issue to raise awareness and stress the importance of responding to alarms and removing faulty batteries from service. • Medtronic identified an interaction between the battery software and an internal component that is causing an increase in battery electrical faults.

Date	Description
	Batteries with a battery electrical fault may be unable to power the controller, unable to accept charge from the battery charger, and/or appear to remain charged when in use. Medtronic has replaced the internal component for all new batteries being manufactured and is in the process of seeking regulatory approval for a change to the battery software.
June 2022	Medtronic issued an Urgent Medical Device Correction to inform health care providers who are following a patient with a pump in the subset identified at higher risk of experiencing a failure to restart that a controller with modified software is available as a back-up if the pump has stopped and the standard controller is unable to restart the pump. The pump failure to restart issue is the same issue that is described in the December 2021 communication.
May 2022	Medtronic issued an Urgent Medical Device Correction to inform health care providers of a welding defect affecting internal HVAD Battery components from a single lot (429 batteries total). Medtronic is replacing the affected batteries with new product and has implemented actions to improve control of the welding process.
April 2022	Medtronic issued an Urgent Medical Device Correction to inform health care providers of a pump weld defect that may present clinical signs and symptoms that resemble pump thrombosis. Medtronic is conducting an investigation to identify which HVAD pumps may be affected.
March 2022	Medtronic issued an Urgent Medical Device Communication to inform health care providers of a Finnish and Turkish language translation issue in the controller and monitor displays. These errors are also present in the Instructions for Use, Patient Manual, and Emergency Responder Guide.
March 2022	Medtronic issued an Urgent Medical Device Communication to provide information correcting errors and inconsistencies, such as incorrect figures and translations, that were identified in the Instructions for Use, Emergency Responder Guide, and Patient Manual.
February 2022	Medtronic issued an Urgent Medical Device Communication to inform health care providers that Medtronic has updated the cleaning instructions for the Controller AC Adapter, DC Adapter, and Battery to provide clarity to avoid cleaning the power source connector pins, as this could remove the lubricant that is applied to the pins as a mitigation for power switching.
December 2021	Medtronic issued an Urgent Medical Device Communication to provide an update on the failure rates associated with the pump failure to restart and additional data to assist in clinical decision-making for patients with a pump in the subset identified at higher risk of failure. Medtronic first issued an Urgent Medical Device Communication for this issue in December 2020. In May 2021, Medtronic also issued an Urgent Medical Device Communication to provide updated information regarding the December 2020 communication to assist health care providers in clinical decision-making regarding controller exchanges.
August 2021	Medtronic issued an Urgent Medical Device Communication to indicate that it may be more difficult to pull back the driveline cover after completion of a Driveline Strain Relief Repair.
June 2021	Medtronic issued an Urgent Medical Device Communication regarding the retrieval of a single non-implanted HVAD Pump Implant Kit containing a pump that did not meet the lower control limit for impeller shroud height.
June 2021	Medtronic issued an Urgent Medical Device Communication to inform health care providers that Medtronic has stopped the distribution and sale of its HVAD System.

Abiomed BVS® 5000 Biventricular Support System/Abiomed AB 5000 Circulatory Support System (AbioMed Cardiovascular, Inc.): The Abiomed BVS 5000 system received FDA approval through the PMA process on Nov 20, 1992 (P900023). On April 28, 2003, FDA PMA approval (P900023/S037) was given for the addition of the AB 5000 pneumatic drive console to the BVS 5000 system. The device can be used either in the hospital or for transport between hospitals. The modified device, marketed as Abiomed AB 5000 circulatory support system, received FDA approval through the PMA process on September 24, 2003 (P900023/S038). According to the approval order statement, it is indicated for use in patients with reversible ventricular dysfunction who have undergone successful cardiac surgery and subsequently develop low cardiac output, or patients with acute cardiac disorders leading to hemodynamic instability. The intent of AB 5000 system therapy is to provide circulatory support, restore normal hemodynamics, reduce ventricular work, and allow the heart time to recover adequate mechanical function.

Thoratec® Paracorporeal Ventricular Assist Device (PVAD™) System and TLC-II Portable VAD Driver: (Thoratec Corporation, Pleasanton, CA): On November 26, 2003 FDA approval through the PMA process was granted to expand the indications for use for the Thoratec VAD System (P870072/S026). The device is approved for post-cardiotomy patients who are unable to be weaned from cardiopulmonary bypass and as a bridge to transplant in patients who are candidates for cardiac transplantation, are at imminent risk of dying, and have a dependence on or incomplete response to vasopressor support. When used with the portable VAD driver, the device is intended for use for transportation of patients via ground ambulance, fixed wing aircraft or helicopter, and can also be used to allow suitably-qualified patients to take off-site excursions within a two-hour travel radius of the hospital in the company of a trained caregiver. On August 3, 2004, supplemental approval was given (P870072/S027) for a modified model of the device that included an alternate VAD blood pump and marketed under the name, Thoratec Implantable Ventricular Assist Device. Indications for the device remain the same.

HeartMate II® Left Ventricular Assist System (LVAS) (Abbott Medical, Pleasanton, CA): The HeartMate II LVAS received FDA approval through the PMA process on April 21, 2008 (P060040). According to the approval letter, the device is indicated for use as a bridge to transplantation in cardiac transplant candidates at risk of imminent death from non-reversible left ventricular failure. It is intended for use both inside and outside the hospital, or for transportation of VAD patients via ground ambulance, fixed-wing aircraft, or helicopter. The device is an implanted continuous axial flow pump with external components. Electrical power to the implanted pump is delivered through a percutaneous lead that connects to an external system controller. The system controller is powered by a power base unit that connects to AC power, or by two batteries carried or worn by the patient. The HeartMate II LVAS, unlike previously approved VADs, is small in size and can be implanted in patients with a body surface area (BSA) less than 1.5 m^2. On January 20, 2010, the HeartMate II indications for use were expanded to allow use in patients who meet the following criteria (P060040/S005):

- New York Heart Association Class IIIB or IV end stage left ventricular failure
- received optimal medical therapy for at least 45 of the last 60 days
- life expectancy of less than two years
- not a candidate for cardiac transplantation

HeartMate 3™ Left Ventricular Assist System (LVAS) (Abbott Medical, Pleasanton, CA): The HeartMate 3 LVAS received FDA PMA approval on August 23, 2017 (P160054). This device is indicated for providing short-term hemodynamic support (e.g., bridge to transplant or bridge to myocardial recovery) in patients with advanced refractory left ventricular heart failure. In October 2018, the FDA approved a PMA supplement for the HeartMate 3 LVAS that expanded the indication to include long-term mechanical circulatory support (P160054/S0008). The device is indicated for

providing short- and long-term mechanical circulatory support (e.g., as bridge to transplant or myocardial recovery, or destination therapy) in patients with advanced refractory left ventricular heart failure.

CentriMag® Blood Pump (Abbott, Pleasanton, CA): The CentriMag Blood Pump (originally marketed by Levitronix LLC) received FDA approval through the 510(k) process in 2003 (K020271). According to the 510(k) summary, it is indicated to pump blood through the extracorporeal bypass circuit for extracorporeal circulatory support for periods appropriate to cardiopulmonary bypass (up to six hours). It is also indicated for use in extracorporeal circulatory support systems (for periods up to six hours) not requiring complete cardiopulmonary bypass (e.g., valvuloplasty, circulatory support during mitral valve reoperation, surgery of the vena cava or aorta, liver transplants etc).

The CentriMag Blood Pump also received FDA Humanitarian Device Exemption (HDE) approval on October 7, 2008 (H070004). According to the original HDE approval, the CentriMag Blood Pump is intended to provide temporary circulatory support for up to fourteen days for patients in cardiogenic shock due to acute right ventricular failure. The device is contraindicated in patients who are unable or unwilling to be treated with heparin or an appropriate alternative anticoagulation and for use as a cardiotomy suction device. Although right ventricular heart failure is infrequent, it may occur following cardiac surgery, myocardial infarction (MI), heart transplantation, or implantation of an LVAD. The device is intended to keep the patient alive until the heart recovers, the patient undergoes a heart transplant, or a long-term VAD is implanted. The CentriMag is a continuous flow, centrifugal-type rotary blood pump. It is unique in that it is designed to operate without mechanical bearings or seals. This is possible because the motor levitates the rotor (i.e., the spinning component of the device) magnetically. On November 12, 2008, the HDE for the CentriMag was expanded, extending the intended duration of support from 14 days to 30 days.

The CentriMag Circulatory Support System (Abbott, Pleasanton, CA; originally marketed by Levitronix LLC) received FDA PMA approval on December 6, 2019 (P170038). The FDA approved indication is for "unilateral or bilateral circulatory support for up to 30 days to treat post-cardiotomy patients as a bridge to decision when they have failed to wean from cardiopulmonary bypass." Contraindications include: use as a cardiotomy suction device and for patients who are unable or unwilling to be treated with an anticoagulant.

PediMag® Blood Pump (Levitronix LLC, Waltham, MA): The PediMag® Blood Pump received FDA approval through the 510(k) pathway in 2009 (K090051). According to the approval summary, the device is intended "for use with the CentriMag Console and Motor to pump blood through a complete extracorporeal bypass circuit for extracorporeal circulatory support for periods appropriate to cardiopulmonary bypass (up to six hours) for surgical procedures such as a mitral valve reoperation. It is also indicated for use in extracorporeal support systems (for periods up to six hours) not requiring complete cardiopulmonary bypass (e.g. valvuloplasty, surgery of the vena cava or aorta, liver transplants etc.). The PediMag Pump can generate a maximum pump flow equal to 1.5 liters per minute, limiting its use to pediatric patients."

The HeartAssist 5® Pediatric VAD: The HeartAssist 5 Pediatric VAD (MicroMed Cardiovascular, Inc., Houston, TX), formerly called The DeBakey VAD Child, received FDA Humanitarian Device Exemption (HDE) approval on June 10, 2003 (H030003). The DeBakey VAD HDE approval was based on a review of data from 190 adults who were implanted with the DeBakey VAD. According to the FDA Summary of Safety and Probable Benefit, the DeBakey VAD Child is expected to provide the same benefits for children that the adult version has provided for adults, with flow rates that will meet the level of output required to support pediatric patients. The FDA Summary of Safety and Probable Benefit states that the DeBakey VAD Child is indicated to provide

temporary left side mechanical circulatory support as a bridge to cardiac transplantation for pediatric patients who meet all of the following criteria:

- age 5–16
- body surface area (BSA) ≥ 0.7 m^2 and < 1.5 m^2
- in NYHA Class IV end-stage heart failure
- refractory to medical therapy
- listed candidate for cardiac transplantation

The following contraindications are listed in the FDA Instructions for Use:

- patients under age five or with BSA < 0.7 m^2
- patients suffering from right ventricular failure unresolved by medical therapy
- patients with a primary coagulopathy or platelet disorders
- prior surgery where apical cannulation, pump replacement or graft anastomosis is not feasible

Berlin Heart EXCOR Pediatric Ventricular Assist Device (Berlin Heart, Inc., Woodlands, TX): The Berlin Heart EXCOR Pediatric VAD, formerly known as EXCOR® Pediatric Ventricular Assist Device (EXCOR), received FDA Humanitarian Device Exemption (HDE) approval on December 16, 2011 (H100004). Berlin Heart then received PMA approval for the device on June 7, 2017 (P160035). The device is intended to provide mechanical circulatory support as a bridge to cardiac transplantation for pediatric patients. Pediatric patients with severe isolated left ventricular or biventricular dysfunction who are candidates for cardiac transplantation and require circulatory support may be treated using the EXCOR. Contraindications to the device include: an inability to tolerate systemic anticoagulation therapy, MRI, and aortic valve regurgitation that cannot be repaired at the time of implantation. Additionally, the device should not be used as a total artificial heart.

Literature Review

Bridge to Recovery: VADs have been used since the 1970s as a bridge to recovery for patients with potentially reversible left ventricular dysfunction. Patients who undergo cardiac surgical procedures are at risk for myocardial injury because of myocardial stunning and ischemia, insufficient myocardial protection, reperfusion injury, and cardiac arrhythmias. Patients who have had persistent or significant dysfunction prior to the surgery are less likely to be weaned from device support, while those who had sufficient myocardial reserve prior to surgery may only require a few days of temporary support. In general, patients in profound shock with end-organ dysfunction and biventricular heart failure need early, effective support to avoid permanent end-organ damage and increase their chances of survival. Devices that provide full ventricular support can reestablish nearly normal hemodynamics and have the potential to allow myocardial recovery. If prolonged support is anticipated, a longer-term biventricular device may be implanted, or a longer term LVAD may be used in conjunction with a short-term RVAD device.

VADs have also been shown to be effective as a bridge to recovery in patients with acute myocarditis, particularly in young patients. It is difficult to determine which patients will recover after short-term support and which patients will need long-term device therapy. For this reason, a long-term device may be inserted, and the device can be explanted if hemodynamic recovery is sufficient or left in place as a bridge to transplantation.

There is adequate evidence in the published medical literature to demonstrate that VADs can be effective when used on a short-term basis in the acute care setting as a bridge to recovery for patients in acute cardiogenic shock or acute myocarditis and for patients following cardiac surgery who cannot be weaned from cardiopulmonary bypass. Patients must, at a minimum, meet the

United States Food and Drug Administration (FDA)-defined, device-specific inclusion and exclusion criteria.

Bridge to Transplantation in Adults: Several published studies have evaluated LVADs as a bridge to transplantation. There is adequate evidence that VADs improve hemodynamic and functional status when used as a bridge to cardiac transplantation. Patients must, at a minimum, meet the FDA-defined, device-specific inclusion and exclusion criteria (Mehra, et al., 2017; Slaughter, et al., 2013; Aaronson, et al., 2012; Pagani, et al., 2009; Frazier, et al., 2001).

The HeartMate 3 received market approval in the European Union in 2015 following completion of a multicenter study. After reaching the six-month study endpoint, patients continue to be followed for two years with the one-year results presented by Krabatsch et al. (2017). The prospective uncontrolled trial (n=50) including adults with advanced heart failure and ejection fraction ≤ 25%, cardiac index ≤ 2.2 L/min/m^2 while not on inotropes, or inotrope dependent, or on optimal medical management for 45/60 days. A total of 54% bridge to transplant (BTT) and 46% destination therapy (DT). At one year, 74% of the patients remain on support, 18% expired, 6% transplanted, and 2% explanted. The adverse events include 12% gastrointestinal bleeding, 16% driveline infections, 18% strokes, and 2% outflow graft thrombosis. There was no hemolysis, pump thrombosis or pump malfunction through one year. The 30-day, six-month, and 12-month survival rates for this cohort were 98, 92, and 81%, respectively**.**

Mehra et al. (2017) conducted a randomized multicenter controlled trial (n=294) assigning patients with advanced heart failure to receive either the HeartMate 3 (n=152) or HeartMate 2 (n=142) LVAS. The trial included patients age ≥ 18 years; body surface area (BSA) ≥ 1.2 m^2; NYHA Class III with dyspnea upon mild physical activity or NYHA Class IV; LVEF ≤ 25%; Inotrope dependent OR cardiac index (CI) < 2.2 L/min/m^2, while not on inotropes and patient must also meet one of the following: On optimal medical management, based on current heart failure practice guidelines for at least 45 out of the last 60 days and are failing to respond; advanced heart failure for at least 14 days AND dependent on intra-aortic balloon pump (IABP) for at least 7 days. The primary end point was a composite of survival free from disabling stroke or survival free from reoperation to replace or remove the device at six months after implantation. At six months post implantation, 86% of patients in the HeartMate 3 arm achieved success in the composite primary endpoint as compared to 77% of patients in the HeartMate II arm, thus demonstrating non-inferiority of HeartMate 3 to HeartMate II. There were no significant between-group differences in the rates of death or disabling stroke, but reoperation for pump malfunction was less frequent in the HeartMate 3 group than in the HeartMate 2 (p=0.002). Suspected or confirmed pump thrombosis occurred in no patients in the HeartMate 3 group and in 14 patients (10.1%) in the HeartMate 2 group.

In a retrospective study (n=24), Ozturk et al. (2017) compared second and third generation LVADs. The study results revealed no significant differences in death rates and surgical revision rates between the LVADs. The HeartMate 3 group had significantly shorter surgical times and required fewer blood transfusions in the postoperative setting than the HeartMate 2 group. The authors reported that the HeartMate 3 LVAD was a safe and effective alternative in treating end-stage HF.

Uriel et al. (2017) used data from the MOMENTUM 3 trial to assess the following secondary endpoints: nonsurgical bleeding, thromboembolic event, pump thrombosis, and neurological event. At six months, the HeartMate 3 group had significantly fewer overall adverse events than the HeartMate II group.

Thomas et al. (2011) reported patient outcome data for a cohort of patients who received the CentriMag device for treatment of primary allograft failure in United Kingdom transplant centers.

Of 572 heart transplants, 38 (6.8%) were implanted with the CentriMag device. Four of these patients received concurrent ECMO and were excluded from analysis. There were no significant differences in transplant characteristics between the patients who received CentriMag support and those who did not. Twelve patients were explanted; nine survived and three died shortly thereafter. Five patients underwent acute re-transplantation; two survived and three died. Seventeen patients died on support. The 30-day and 1-year survival rates were 50% (95% confidence interval (CI) 32-65%) and 32% (95% CI 18-48%), respectively. Patients who had a bridge-to-transplant ventricular assist device (VAD) prior to transplant had significantly better survival than those who did not (1-year survival 71% vs 22%, p = 0.029). The rate of adverse events was high; 24 of 30 patients experienced at least one adverse event. Bleeding was the most common adverse event. Although the rate of adverse events was high, the authors stated that most patients would have died without mechanical support.

Bridge to Transplantation in Children: Extracorporeal membrane oxygenation support (ECMO) has been routinely used in pediatric patients awaiting heart transplantation, but this treatment is limited to the inpatient setting. Waiting times for allografts frequently exceed the period of time a patient can be supported on ECMO. The use of long-term mechanical circulatory support has therefore increased over the past ten years as a bridge to transplantation for pediatric patients (Blume et al., 2006).

There is adequate evidence that VADs improve hemodynamic and functional status when used as a bridge to cardiac transplantation in children. Patients must, at a minimum, meet the FDA-defined, device-specific inclusion and exclusion criteria (Rohde, et al., 2019; Almond, et al., 2013; Fraser, et al., 2012; Morales, et al., 2011; Blume, et al., 2006).

Although most studies are nonrandomized and many are retrospective, there is sufficient evidence that LVADs can improve functional and hemodynamic status and are associated with higher survival rates when compared to optimal medical therapy. In addition, improved post-transplant survival rates are seen in patients who received LVADs. This benefit of improved post-transplant survival is likely due to the efficient circulatory support provided by the device, as well as the fact that patients stabilized by LVAD implantation can wait for an optimal organ match. LVADs have therefore become an accepted tool to halt further deterioration, decrease the likelihood of death before transplantation, and improve long-term survival and quality of life in selected patients.

Jordan et al. (2015) conducted a multicenter prospective cohort study to report neurological events in children supported with the Berlin Heart EXCOR device. The study consisted of all 204 children implanted with the Berlin Heart EXCOR device at 47 centers in North America. There were 73 neurological events in 59 patients, with 29% of the cohort experiencing ≥1 neurological event. Events included 52 strokes in 43 patients (21% of the cohort). The neurological event rate was 0.51 events per 100 patient-days. Many of the neurological events occurred early in the course of support, with 30 events recorded during the first 14 days of support. The mortality rate in participants with at least 1 neurological event was 42% (25 of 59), significantly higher than the 18% mortality rate (26 of 145) for those who did not have a neurological event (p=0.0006). Risk-factor analysis did not identify significant preimplantation predictors of neurological injury.

According to the FDA Summary of Safety and Probable Benefit, the results of the Berlin Heart EXCOR Investigational Device Exemption (IDE) study (Fraser, et al., 2012) demonstrated that a majority of primary study patients survived to successful weaning or cardiac transplantation with acceptable neurological status. The study also demonstrated, however, that use of the EXCOR device is accompanied by significant risks. A high rate of neurological events was seen in the EXCOR primary study patients; 30% experienced an ischemic neurological event. There also appeared to be a high incidence of pump thrombus. There was a higher failure rate in patients who did not meet the strict eligibility criteria and in patients implanted at non-study-centers.

According to the summary, data from the IDE trial demonstrate that the device is safe as defined by the safety endpoint, and considering the other clinically available alternatives, the device provides probable benefit to this very limited patient population. The Circulatory System Devices Panel noted that survival rates were in favor of the EXCOR device compared to the control group treated with extracorporeal membrane oxygenation support (ECMO), and patients were able to remain on the device for longer periods of time compared to the patients on ECMO. The panel states that the device meets a critical need for patients with end stage heart failure who are awaiting a transplant. The panel agreed that the device provided a reasonable assurance of safety and that the probable benefit of the device outweighed the known risks. A post-approval study will include follow-up of current IDE study patients and enrollment of a new cohort with important baseline data and follow-up beyond explanation.

Destination Therapy: There is adequate evidence in the published medical literature that LVAD therapy is effective as destination therapy for selected end-stage heart failure patients who are not eligible for heart transplantation (Rogers, et al., 2017; Rogers, et al., 2010; Slaughter al., 2009; Rose, et al., 2001). Patients must, at a minimum, meet the FDA-defined, device-specific inclusion and exclusion criteria.

Mehra et al. (2018) conducted a randomized noninferiority and superiority trial, comparing the centrifugal-flow HeartMate 3 LVAS (n=190) with the axial-flow HeartMate II LVAD (n=176) in patients with advanced heart failure, irrespective of the intended goal of support (bridge to transplantation or destination therapy). The composite primary end point was survival at two years free of disabling stroke or survival free of reoperation to replace or remove a malfunctioning device. In the intention-to-treat population, the primary end point occurred in 79.5% (n=151) of the HeartMate 3 LVAS population and 60.2% (n=106) of the HeartMate II LVAD population. Reoperation for pump malfunction was less frequent in the HeartMate 3 LVAS group (1.6%; 3 participants) than in the HeartMate II LVAD group (17.0%; 30 participants). Among the two groups, the rates of disabling stroke were similar, but the overall rate of stroke was lower in the HeartMate 3 LVAS group than in the HeartMate II LVAD group (10.1% vs 19.2%). The authors concluded that in patients with advanced heart failure, a fully magnetically levitated centrifugal-flow pump was superior to a mechanical-bearing axial-flow pump with regard to survival free of disabling stroke or reoperation to replace or remove a malfunctioning device.

Rogers et al. (2017) conducted a prospective, randomized, controlled, multicenter clinical trial (n=466) in patients with advanced heart failure who were ineligible for heart transplantation. Subjects in the ENDURANCE™ Destination Therapy trial were randomly assigned in a 2:1 ratio, to receive either the study (HeartWare HVAD) centrifugal-flow LVAD or control (HeartMate II) axial-flow LVAD. The primary end point was survival at two years free from disabling stroke or device removal for malfunction or failure. The intention-to treat-population included 297 participants assigned to the study device and 148 participants assigned to the control device. The primary end point was achieved in 164 patients in the study group and 85 patients in the control group. The analysis of the primary end point showed noninferiority of the study device relative to the control device with estimated success rates, 55.4% and 59.1%, respectively (p=0.01 for noninferiority). More patients in the control group than in the study group had device malfunction or device failure requiring replacement (16.2% vs. 8.8%), and more patients in the study group had strokes (29.7% vs. 12.1%). Quality of life and functional capacity improved to a similar degree in the two groups.

Cardiogenic Shock: John et al. (2011) conducted a multi-institutional study evaluate safety, effectiveness, and outcomes of the CentriMag in patients with cardiogenic shock following cardiotomy (n=12), myocardial infarction (n=14) or with right ventricular failure after left ventricular assist device placement (n=12). Devices were implanted in left (n=8), right (n=12), or biventricular (n=18) configurations. CentriMag support was continued until patients recovered,

received a transplant, or received an implantable long-term VAD. The mean support duration for the entire cohort was 13 days (range 1–60 days), with 47% of patients surviving 30 days following removal Complications included bleeding (21%), infection (5%), respiratory failure (3%), hemolysis (5%), and neurologic dysfunction (11%). There were no device failures. The authors stated that in this preliminary study, the CentriMag VAS is capable of providing biventricular support for patients with medically refractory acute cardiogenic shock with an acceptable survival.

Percutaneous Ventricular Assist Devices:
Percutaneous ventricular assist devices (VADs), also referred to as percutaneous circulatory support devices, have been proposed as an alternative to a traditional VAD or intra-aortic balloon pump (IABP) for short-term partial or total hemodynamic support. Unlike traditional VADs, percutaneous VADs are minimally invasive and do not require surgical implantation, and unlike IABP, percutaneous VADs provide hemodynamic support independent of left ventricular function. Percutaneous VADs have been proposed for use during emergent procedures for patients in acute heart failure caused by left ventricular dysfunction and/or cardiogenic shock. They have also been proposed as an alternative to IABP for use in high-risk percutaneous coronary intervention (PCI) procedures.

The severity of heart failure is a key factor in assessing the need for VAD use. The New York Heart Association functional classification system, below, is the most frequently used measure of heart failure and is included in the FDA approval criteria for most VADs.

- Class I. Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.
- Class II. Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.
- Class III. Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.
- Class IV. Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

Many cardiologists further stratify Class III patients with a sub-classification of IIIA to indicate no dyspnea at rest, and IIIB to indicate recent dyspnea at rest.

U.S. Food and Drug Administration (FDA)
TandemHeart® PTVA® System (CardiacAssist, Inc., Pittsburgh, PA): The TandemHeart PTVA System consists of three components: the TandemHeart Transseptal Cannula Set-EF which received FDA approval through the 510(k) process on January 17, 2006 (K052570), the TandemHeart® Escort™ Controller which received FDA approval through the 510(k) process on August 22, 2006 (K061369), and the TandemHeart PTVA Blood Pump. The Controller is a reusable, microprocessor-based pump motor drive and infusion system. The controller generates the signals required to power the drive motor of the blood pump, which turns the impeller to propel blood through the pump. According to the FDA 510(k) summary, the TandemHeart PTVA System is intended for extracorporeal circulatory support using an extracorporeal bypass circuit. The intended duration of use is for periods appropriate to cardiopulmonary bypass, up to six hours. It is also intended to be used as an extracorporeal circulatory support system (for periods up to six hours) for procedures not requiring complete cardiopulmonary bypass (e.g., valvuloplasty, mitral valve reoperation, surgery of the vena cava and/or aorta, liver transplant).

On March 4, 2016, the Protek Duo 31 Fr. Veno-Venous Cannula set received FDA 510(k) approval for "use as a single cannula for both venous drainage and reinfusion of blood via an internal jugular vein during extracorporeal life support procedures."

Impella Recover® LP 2.5 Percutaneous Cardiac Support System, Impella 2.5 Plus/Impella CP™ (Abiomed, Inc., Danvers, MA): The Impella Recover LP 2.5 Percutaneous Cardiac Support System received FDA 510(k) approval on May 30, 2008 (K063723). The system provides circulatory support with the ability to deliver an anticoagulant through an infusion system. It consists of a catheter which contains an integrated pump motor/infusate lumen; integrated intravascular pressure lumen and integral cannula; a controller/console; infusion system; and accessories. The Impella Recover is intended for partial circulatory support using an extracorporeal bypass control unit for periods up to six hours. It is also intended to be used to provide partial circulatory support (for periods up to six hours) during procedures not requiring cardiopulmonary bypass. A revised version of the Impella 2.5 (K063723), the Impella 2.5 Plus, received 510(k) approval on September 5, 2012 (K112892). The updated device includes a slight increase in the diameter of the inflow cannula, impeller and pump housing, allowing 30% higher flow. It is otherwise identical to the predicate device, the Impella 2.5. The Impella 2.5 Plus will be marketed as the Impella CP™ (Cardiac Power) in the U.S. Indications for use remain unchanged.

Impella 5.0® Catheters (Abiomed, Inc., Danvers, MA): The Impella 5.0 Catheters received FDA approval through the 510(k) process on April 16, 2009 (K083111). The Impella 5.0 catheter family is an extension of the Impella Percutaneous Cardiac Support line. There are two versions of Impella 5.0: the Impella 5.0 LP is inserted through the femoral artery via cutdown and the Impella 5.0 LD is inserted through the aorta. The only difference between the two catheters is the shape of the inflow cannula. The characteristics of the Impella 5.0 are similar to the Impella 2.5, but the larger pump in the Impella 5.0 permits a higher flow range, up to 5 liters per minute.

Impella 2.5 Percutaneous Ventricular Assist Device (Abiomed, Inc., Danvers, MA): On March 23, 2015, the FDA issued Premarket Approval (PMA) for the Impella 2.5 percutaneous ventricular assist device (P140003). The device is indicated as a temporary (≤ 6 hours) ventricular support device for use during high-risk percutaneous coronary interventions (PCI) performed in elective or urgent, hemodynamically stable patients with severe coronary artery disease and depressed left ventricular ejection fraction, when a heart team, including a cardiac surgeon, has determined high-risk PCI is the appropriate therapeutic option. Use of the Impella 2.5 in these patients may prevent hemodynamic instability which can result from repeat episodes of reversible myocardial ischemia that occur during planned temporary coronary occlusions and may reduce peri- and postprocedural adverse events. On December 1, 2016 Abiomed received PMA approval (P140003/S008) to add the Impella CP to the list of devices approved for use during high-risk PCI.

On April 7, 2016, Abiomed received additional PMA approval (P140003/S004/S005) to expand the indication for use to include the treatment of ongoing cardiogenic shock that occurs immediately following acute myocardial infarction and to include additional Impella Catheters for this indication. To accommodate a range of cardiac flow requirements, different sized Impella Support Catheters are available. The peripherally placed catheters are the Impella 2.5, the Impella CP and the Impella 5.0, which have blood pump diameters of 12F, 14F and 21F, respectively. In addition, a fourth 21F surgically placed Impella Catheter, the Impella LD, is available. The Impella 2.5, Impella CP, Impella 5.0, and Impella LD catheters, when used in conjunction with the Automated Impella Controller, are indicated for short term use (< 4 days for the Impella 2.5 and Impella CP, and < 6 days for the Impella 5.0 and Impella LD) for the treatment of ongoing cardiogenic shock that occurs immediately (< 48 hours) following acute myocardial infarction or open heart surgery as a result of isolated left ventricular failure that is not responsive to optimal medical management and conventional treatment measures. On February 7, 2018 Abiomed received additional PMA approval (P140003/S018) to expand the indication for use for the Impella Ventricular Support

Systems. The indications for use state that the Impella 2.5, Impella CP, Impella 5.0, and Impella LD Catheters, in conjunction with the Automated Impella Controller, are temporary ventricular support devices intended for short term use (≤4 days for the Impella 2.5 and Impella CP, and ≤6 days for the Impella 5.0 and Impella LD) and indicated for the treatment of ongoing cardiogenic shock that occurs:

- immediately (<48 hours) following acute myocardial infarction or open heart surgery; or
- in the setting of cardiomyopathy, including peripartum cardiomyopathy, or myocarditis as a result of isolated left ventricular failure that is not responsive to optimal medical management and conventional treatment measures.

The FDA Instructions for Use states the Impella Ventricular Support Systems are contraindicated for patients with the following conditions:

- mural thrombus in the left ventricle
- mechanical aortic valve or heart constrictive device
- aortic valve stenosis/calcification (equivalent to an orifice area of 0.6 cm^2 or less)
- moderate to severe aortic insufficiency (echocardiographic assessment graded as ≥ +2)
- severe peripheral arterial disease that precludes the placement of an Impella Catheter
- significant right heart failure
- combined cardiorespiratory failure
- presence of an atrial or ventricular septal defect (including post-infarct VSD)
- left ventricular rupture
- cardiac tamponade

On February 8, 2018 Abiomed received additional PMA approval (P140003/S027) to remove the reference to "depressed left ventricular ejection fraction" from the indications for use statement for the Impella 2.5 and Impella CP Systems.

Impella 5.5 With SmartAssist (Abiomed, Inc., Danvers, MA): The Impella 5.5 With SmartAssist received FDA approval through the Premarket Approval (PMA) process on September 24, 2019 (P140003/S050). The approval, which is a supplement for the Impella 2.5 (P140003), increased the lumen which allows a higher flow rate of up to 6.0 liters per minute. The SmartAssist module provides weaning protocols and allows physicians and providers to view the controller interface via a Health Insurance Portability and Accountability Act (HIPAA) complaint website. The Impella 5.5 with SmartAssist is indicated for short term use (≤ 14 days) in a patient with cardiogenic shock immediately after (within 48 hours) an acute myocardial infarction, open heart surgery or cardiomyopathy.

Impella RP System (Abiomed, Inc., Danvers, MA): The Impella RP System received FDA Humanitarian Device Exemption (HDE) approval on January 23, 2015 (H140001) based on the results of the RECOVER RIGHT study and then received PMA approval on September 20, 2017 (P17001) indicating that this device is approved for providing circulatory assistance for up to 14 days in pediatric or adult patients with a body surface area ≥ 1.5m^2 who develop acute right heart failure or decompensation following left ventricular assist device implantation, myocardial infarction, heart transplant, or open-heart surgery. The Impella RP System is a minimally invasive, miniaturized percutaneous circulatory support system for the right ventricle. It is comprised of three components: the Impella RP Catheter, a 22 Fr micro-axial flow pump catheter and its accessories; the Automatic Impella Controller (AIC), a reusable extracorporeal drive console; and the Impella Purge Cassette, an infusion pump used to flush the Impella RP Catheter. The Impella RP System is contraindicated for patients with the following conditions:

- disorders of the pulmonary artery wall that would preclude placement or correct positioning of the Impella RP device
- mechanical valves, severe valvular stenosis or valvular regurgitation of the tricuspid or pulmonary valve
- mural thrombus of the right atrium or vena cava
- anatomic conditions precluding insertion of the pump
- presence of a vena cava filter or caval interruption device, unless there is clear access from the femoral vein to the right atrium that is large enough to accommodate a 22 Fr catheter

Literature Review

High-Risk Percutaneous Intervention: Cohen et al. (2015) conducted a multicenter retrospective observational study comparing the characteristics, procedures, and outcomes of high-risk PCI supported by a microaxial pump (Impella 2.5) in a multicenter registry versus the randomized PROTECT II trial. A total of 637 were included from the registry. Of them, 339 patients would have met enrollment criteria for the PROTECT II trial. These were compared with 216 patients treated in the Impella arm of PROTECT II. Compared to the clinical trial, registry patients were older (70 ± 11.5 vs 67.5 ± 11.0 years); more likely to have chronic kidney disease (30% vs 22.7%), prior myocardial infarction (69.3% vs 56.5%), or prior bypass surgery (39.4% vs. 30.2%); and had similar prevalence of diabetes, peripheral vascular disease, and prior stroke. Registry patients had more extensive coronary artery disease (2.2 vs 1.8 diseased vessels) and had a similar Society of Thoracic Surgeons predicted risk of mortality. At hospital discharge, registry patients experienced a similar reduction in New York Heart Association class III to IV symptoms compared to trial patients. Registry patients had a trend toward lower in-hospital mortality (2.7% vs 4.6, p=0.27).

O'Neill et al. (2012) conducted a prospective multicenter randomized trial (the PROTECT II study) to assess whether a high-risk PCI strategy with the support of the Impella 2.5 device would result in better outcomes than a revascularization strategy with IABP support (n=452). Included patients were age 18 or older and scheduled to undergo a non-emergent PCI on an unprotected left main or last patent coronary vessel, with a left ventricular ejection fraction (LVEF) of ≤ 35%, or with 3-vessel disease and LVEF ≤ 30%. Patients were randomized to IABP (n=226) or Impella 2.5 (n=226) during nonemergent PCI. The primary endpoint was the composite rate of intra-and post-procedural major adverse events (MAE) at discharge or 30-day follow-up, whichever was longer. Between November 27, 2007 and December 6, 2010, 452 patients were enrolled; 69% of the planned enrollment. After review of the available interim data, the Data and Safety Monitoring Board (DSMB) recommended the early discontinuation of the study for futility based on the observed conditional power of the 30-day results of the first 327 patients and the assumed similar trend for the remaining patients to be included in the study. (When enrollment ceased, an additional 125 patients had been enrolled beyond the initial 327 patients). Based on an intent-to-treat analysis, there was no statistically significant difference in the primary endpoint, MAE at 30 days, between patients in the Impella arm (35.1%) and the IABP arm (40.1%) (p=0.277). A follow-up of the composite primary end point was also performed at 90 days, and showed a trend toward decreased MAE in the Impella arm (40.6%) compared to the IABP arm (49.3%) (p=0.066) in the intent-to-treat population, and 40.0% vs. 51.0% (p=0.023), in the per-protocol population, respectively. The authors acknowledged that because the difference in 30-day MAE did not reach statistical significance for the entire study, the analysis of 90-day events remains exploratory.

Data from the USpella Registry regarding experience with the Impella 2.5 in complex high-risk PCI procedures was published by Maini et al. in 2012 (n=175). The primary endpoint was the incidence of major adverse cardiac events (MACE) at 30 days. Secondary endpoints included safety, efficacy, and patient outcomes at 12 months. PCI was elective in 53% of cases and urgent

in 47%. A majority of patients (69%) had ejection fraction < 35%, and 66% were in NYHA Class III or IV heart failure. Multi-vessel disease was present in 89% of patients, and 56% had an unprotected left main or last patent coronary artery. Seven patients died within 30 days. Angiographic revascularization was successful in 99% of patients overall, and in 90% of those with multi-vessel revascularization. SYNTAX scores (a measure of the complexity of coronary artery disease), ejection fraction, and functional status all improved significantly. The rate of overall MACE was 8% at 30 days, and survival was 96%, 91%, and 88% at 30 days, six months, and 12 months, respectively. The authors cited limitations of the study, including the fact that the observational design of the registry cannot establish causality or efficacy compared to a no-device approach, and that patient selection may limit extrapolation of these findings to a more general patient population.

A retrospective case series (Alasnag et al., 2011) evaluated the safety and feasibility of prophylactic use of the Impella 2.5 during high-risk PCI (n=60). All patients were either considered inoperable by the cardiac surgeons or declined bypass surgery, and presented with multiple risk factors, including hypertension, diabetes, chronic pulmonary disease, prior MI, and prior bypass surgery, and 45% presented with acute coronary syndrome. The mean ejection fraction was 23% ± 15%. The majority of patients had multi-vessel disease, and 60% had left main disease. An angiographic success rate of 96% was achieved. The device was used for an average of 38 ± 15 minutes and provided a mean blood flow of 2.1 ± 0.2 liters/minute. Hemostasis was achieved in 56 of 60 patients; endovascular tamponade, manual compression, and vascular surgery were used for two, one, and one patient, respectively. The 30-day mortality rate was 5%, and rates of MI, stroke, target lesion revascularization and urgent bypass surgery were 0%. The authors concluded that use of the Impella 2.5 during high-risk PCI outside the controlled environment of a clinical trial is safe and feasible, but acknowledged study limitations, including the retrospective nature of the trial, and the fact that the determination that patients were sufficiently high risk to benefit from the use of the Impella was made by the cardiologist performing the procedure, and was not subject to rigid criteria. The authors stated that randomized controlled trial data is needed to quantify the benefit of Impella 2.5 support during high-risk PCI compared to that of the IABP.

The Europella Registry (Sjauw, et al., 2009) evaluated the safety and feasibility of left ventricular support with the Impella 2.5 during high-risk PCI (n=144). Patients were older (62% > 70), and 54% had a left ventricular ejection fraction (LVEF) ≤ 30%. PCI was considered high risk due to left main disease, last remaining vessel disease, multivessel coronary artery disease, and low LV function in 53%, 17%, 81%, and 35% of cases, respectively. Rates of MI, stroke, bleeding requiring transfusion/surgery, and vascular complications at thirty days were 0%, 0.7%, 6.2%, and 4.0%, respectively. Thirty-day mortality was 5.5%.

A multicenter prospective case series conducted by Dixon, et al. (2009) evaluated the safety and feasibility of the Impella 2.5 system in patients undergoing high-risk PCI (n=20). All patients had LVEF ≤ 35% and underwent PCI on an unprotected left main coronary artery or last patent coronary conduit. The primary safety end point was the incidence of major adverse cardiac events (MACE) at thirty days. The primary efficacy end point was freedom from hemodynamic compromise during PCI (defined as a decrease in mean arterial pressure below 60 mm Hg for more than ten minutes). The mean duration of support was 1.7 ± 0.6 hours (range 0.4–2.5 hours). The incidence of MACE at thirty days was 20%; two patients had a peri-procedural MI, and two died at days 12 and 14. The authors stated that, based on the results of this trial, a pivotal randomized trial is planned to compare the efficacy of prophylactic circulatory support during high-risk PCI with the Impella 2.5 vs. conventional IABP counterpulsation.

Meta-Analysis High-Risk PCI: In a meta-analysis of randomized controlled studies, Shi et al. (2019) compared the use of percutaneous mechanical circulatory support devices during high risk

percutaneous coronary intervention. Comparison was made when intra-aortic balloon pump or a percutaneous mechanical circulatory support device (Impella 2.5, Impella CP or TandemHeart) was used during intervention of PCI. The objective of the study was all-cause mortality at thirty days and six months. Randomized controlled studies (n=16 studies: IABP n=9, pVAD n=7; n=3266 patients) were included if patients were treated with a percutaneous mechanical circulatory support device (pMCSD) during percutaneous coronary intervention (PCI), reported all-cause mortality and adverse events. Studies were excluded when reported as cohort, real-world, cross-sectional surveys, patients undergoing coronary artery bypass grafting (CABG) and any patient treated with systemic thrombolysis. The primary outcome of the study was all-cause mortality. Secondary outcome measures were evidence of reinfarction, acute kidney injury, heart failure, stroke/transient ischemic attack (TIA), embolization, arrhythmia, repeat revascularization and bleeding events. The primary and secondary outcome measured showed intra-aortic balloon pump (IABP) had no statistically significant decrease in 30-day and 6-month all-cause mortality (RR 1.01 95% CI 0.61–1.66; RR 0.88 95% CI 0.66–1.17), reinfarction (RR 0.89 95% CI 0.69–1.14), stroke/transient ischemic attack (RR 1.75 95% CI 0.47–6.42), heart failure (RR 0.54 95% CI 0.11–2.66), repeat revascularization (RR 0.73 95% CI 0.25–2.10), embolization (RR 3.00 95% CI 0.13–71.61), or arrhythmia (RR 2.81 95% CI 0.30–26.11). Compared with IABP, percutaneous ventricular assist devices (pVADs) had no statistically significant decrease in 30-day and six-month all-cause mortality (RR 0.96 95% CI 0.71–1.29; RR 1.23 95% CI 0.88–1.72), reinfarction (RR 0.98 95% CI 0.68–1.42), stroke/TIA (RR 0.45 95% CI 0.1–1.95), acute kidney injury (AKI) (RR 0.83 95% CI 0.38–1.80), or arrhythmia (RR1.52 95% CI 0.71–3.27). pVADS showed a statistically significant decrease in repeat revascularization (RR 0.26 95% CI 0.08-0.83) and statistically significant increase in risk of bleeding compared with IABP (RR 2.85 95% CI 1.72-4.73). Author noted limitations include mild heterogeneity of procedures, protocols and devices used, amalgamation of aggregate patient data, limitation in original data and small number of trials available reporting association between pVADs and repeat revascularization. Larger studies are needed to assess the benefit of percutaneous mechanical circulatory support device use during high risk PCI.

Ait Ichou et al. (2018) conducted a systematic review of randomized controlled trials (RCTs) and observational studies to synthesize the currently available evidence on the effectiveness and safety of the Impella 2.5 or 5.0 devices in high-risk patients undergoing PCI. A total of 20 studies met the inclusion criteria. Those studies consisted of four RCTs [Seyfarth, et al., 2008; O'Neil, et al., 2012; Ouweneel, et al., 2016, 2017] and 16 observational studies, including a total of 1287 patients. All studies were published between 2006 and 2016, and the durations of follow-up ranged from 1-42 months. Ten studies examined prophylactic use of the Impella device among high-risk patients undergoing elective PCI, five examined its use among high-risk patients undergoing emergent PCI, and four examined its use in mixed populations of high-risk patients undergoing elective or emergent PCI. Mean LVEF was low, ranging from 23%-37%, while the percentage of patients with previous MI was variable, ranging from 24%-76%. Overall, patients had multiple co-morbidities and were at high procedural risk. The use of Impella resulted in improved procedural and hemodynamic characteristics in controlled and uncontrolled studies. In controlled studies, the 30-day rates of all-cause mortality and major adverse cardiac events (MACE) were similar across groups. In most uncontrolled studies, the 30-day rates of all-cause mortality were generally low (range: 3.7%–10%), though rates of MACE were slightly higher (range: 5%–20%). The authors concluded that there is limited evidence available concerning the effect of Impella on clinical events, particularly compared to IABP. Although procedural and hemodynamic results appear promising, there remains a need for large, multicenter RCTs to conclusively assess the effectiveness and safety of Impella.

Cardiogenic Shock: Based on the available evidence, the Impella and TandemHeart may be indicated to provide short-term circulatory support for individuals in cardiogenic shock. Although the published evidence is limited and does not demonstrate improved outcomes compared to the

intra-aortic balloon pump, these devices may provide improved hemodynamic support independent of left ventricular function in patients in cardiogenic shock.

Ouweneel et al. (2017) conducted a randomized, prospective, open-label, multicenter study to determine whether a new percutaneous mechanical circulatory support (pMCS) device (Impella CP) decreases 30-day mortality when compared with an intra-aortic balloon pump (IABP) in patients with severe shock complicating AMI. A total of 48 patients with severe cardiogenic shock (CS) complicating AMI were assigned to pMCS (n=24) or IABP (n=24). Severe CS was defined as systolic blood pressure <90 mm Hg or the need for inotropic or vasoactive medication and the requirement for mechanical ventilation. The primary endpoint was 30-day all-cause mortality. At 30 days, mortality in patients treated with either IABP or pMCS was similar (50% and 46%, respectively). At six months, mortality rates for both pMCS and IABP were 50%.

The Impella-EUROSHOCK-registry evaluated the safety and efficacy of the Impella 2.5 in 120 patients with cardiogenic shock after acute MI (Lauten et al., 2013). A total of 14 tertiary cardiovascular centers in five countries across Europe contributed data to the registry. The primary endpoint was mortality at 30 days; the secondary endpoints included change in plasma lactate following institution of hemodynamic support, rate of early major adverse cardiac and cerebrovascular events (MACCE), and long-term survival. Thirty-day mortality was 64.2%. After Impella implantation, lactate levels decreased from 5.8 ± 5.0 millimoles per liter (mmol/L) to 4.7 ± 5.4 mmol/L at 24 hours(p=0.28) and 2.5 ± 2.56 mmol/L (p=0.023) at 48 hours. Early MACCE were reported in 18 (15%) patients. Major bleeding at the vascular access site, hemolysis, and pericardial tamponade occurred in 34 (28.6%), 9 (7.5%), and 2 (1.7%) patients, respectively. Survival was 28.3% after 317 ± 526 days. The authors concluded that in patients with acute cardiogenic shock from acute MI, Impella 2.5 treatment is feasible and results in improved lactate levels, suggesting improved organ perfusion. Thirty-day mortality remained high, however, which likely reflected the last resort character of Impella application in patients with a poor hemodynamic profile and greater imminent risk of death. The authors further concluded that carefully conducted randomized controlled trials are necessary to evaluate the efficacy of Impella 2.5 support in this high-risk patient group.

Kar et al. (2011) evaluated the efficacy and safety of the TandemHeart percutaneous assist device (pVAD) in patients with refractory cardiogenic shock despite IABP and/or high-dose vasopressor support (n=117). Of the 117 patients, 56 (47.9%) underwent active cardiopulmonary resuscitation immediately prior to or at the time of implantation. The average duration of support was 5.8 ± 4.75 days. There was statistically significant improvement in the average cardiac index, systolic blood pressure and mixed oxygen saturation during the period of implantation. Urine output increased, and pulmonary capillary wedge pressure and lactic acid also improved significantly. The mortality rate was 40.2% at 30 days and 45.3% at six months. The authors concluded that the TandemHeart is an effective treatment option for rapidly reversing terminal circulatory collapse, and further prospective randomized controlled trials are warranted to evaluate the efficacy of early pVAD placement in severe refractory cardiogenic shock patients.

A randomized controlled trial by Seyfarth et al. (2008) was conducted to determine whether the Impella 2.5 percutaneous VAD provided superior hemodynamic support compared to the IABP (n=26). After an initial hemodynamic assessment, patients with acute MI and cardiogenic shock were randomized to Impella 2.5 (n=12) or IABP (n=13). One patient died prior to implantation. Patients were immediately transferred to the catheterization lab, and the assigned device was implanted after revascularization therapy. The primary endpoint was the change in cardiac index from baseline to thirty minutes after implantation. The cardiac index of patients in the Impella group was significantly increased after thirty minutes of support compared to the IABP group (p=0.02). The median duration of support was 25 hours in the Impella group and 23 hours in the IABP group. There was one case of acute limb ischemia in the Impella group. Transient hemolysis

was significantly higher in the Impella group, with more packed red blood cells and fresh frozen plasma administered (p=0.18 and p=0.39, respectively). Overall thirty-day mortality was 46% in both groups.

Burkhoff et al. (2006) conducted a randomized controlled trial to determine whether the TandemHeart provided superior hemodynamic support compared to IABP in patients with cardiogenic shock (n=42). Patients from 12 centers presenting within 24 hours of developing cardiogenic shock were treated in an initial roll-in phase (n=9, or randomized to treatment with IABP (n=14) or TandemHeart (n=19).Of the 42 patients, 26 were diagnosed with acute MI. Most of the patients had an IABP in place before randomization. The mean duration of support was 2.5 days. Patients treated with the TandemHeart had significantly greater increases in cardiac index and greater decreases in pulmonary capillary wedge pressure compared to those treated with IABP. There was no significant difference in 30-day overall survival or incidence of adverse events between the two groups; serious adverse events occurred with a frequency of 1.3 per patient in the TandemHeart group and 1.2 per patient in the IABP group. The authors noted that larger scale studies are needed to assess the influence of improved hemodynamics on survival.

Thiele et al. (2005) conducted a randomized controlled trial to evaluate hemodynamic effects of the intra-aortic balloon pump (IABP) compared to the TandemHeart, and to assess mortality in patients with cardiogenic shock complicating acute myocardial infarction (MI). Patients were randomized to treatment with the IABP (n=20) or TandemHeart (n=21). Inclusion criteria were the presence of acute MI and cardiogenic shock with an intention to revascularize the infarcted artery by percutaneous coronary intervention (PCI). Hemodynamic indices at baseline were similar for both groups, except for a higher pulmonary capillary wedge pressure in the IABP group. The primary endpoint, cardiac power index, was improved more effectively with the TandemHeart, ($p<0.001$) compared to the IABP ($p=0.02$) ($p=0.004$ for intergroup comparison). Weaning from the devices was completed using a stepwise approach over a period of four to eight hours. Complications occurred more frequently in the TandemHeart group compared to the IABP group, however. Severe bleeding occurred in 19 TandemHeart patients compared to 8 IABP patients ($p=0.002$), and limb ischemia occurred in 7 TandemHeart patients compared to 0 IABP patients. Thirty-day mortality was similar in both groups (IABP 45% vs. TandemHeart 43%, $p=0.86$). Although this trial did not have the power to detect differences in mortality, there was no trend in mortality benefit for the TandemHeart patients despite the improved hemodynamics.

Meta-Analysis Cardiogenic Shock: Batsides et al. (2018) conducted a systematic review and meta-analysis to investigate the survival outcomes and device-related complications of Impella 5.0 use in patients with cardiogenic shock (CS). Impella 5.0 provides the highest antegrade flow rates among the Impella platform of current left ventricular assist devices. The primary outcome was survival to discharge. The secondary outcomes included survival to explant, 30, 180, and 365 days, survival to next therapy, myocardial recovery, stroke, bleeding, vascular complication, limb ischemia, hemolysis, valve injury, and device malfunction. This meta-analysis included six studies (n=163). Five studies were observational retrospective studies and one was a prospective single arm study. Indications for support included 88 (54.0%) for acute on chronic decompensated heart failure, 35 (21.5%) for postcardiotomy cardiogenic shock, 27 (16.6%) for acute myocardial infarction complicated by cardiogenic shock, and, 13 (8.0%) for cardiogenic shock due to other reasons. The pooled mean and range of the baseline left ventricular ejection fraction and the duration of Impella support was 13.5% (2%–35%) and 8.6 days (1–71 days), respectively. Survival to next therapy was 73.5% in patients supported for acute on chronic decompensated heart failure. The survival to device explant among patients supported for postcardiotomy cardiogenic shock or acute myocardial infarction complicated by cardiogenic shock was 90.2%, and of those, myocardial recovery was achieved in 73.8%. The overall estimated survival to discharge, 30, 180, and 365 days was 73.5%, 72.6%, 62.7%, and 58.4%, respectively. Patients supported for postcardiotomy cardiogenic shock had the highest heart recovery among survivors

to explant (92.1%) and highest survival at 30 (89.5%) and 365 days (69.5%). The pooled rate of stroke, bleeding, vascular complications, limb ischemia, hemolysis, device malfunction was 0.1%, 21.6%, 0.2% 0.2%, 0.7%, 10.7% and 0.2%, respectively. Limitation of this meta-analysis includes study level data and inclusion of studies with heterogeneous cause of CS, study selection bias, definitions, and primary outcomes resulting in heterogeneity when performing a pooled analysis. The retrospective design of the studies included in might contribute to the low rate of complications as the authors might have reported only well documented complications.

Thiele et al. (2017) conducted a meta-analysis of randomized trials to investigate the efficacy and safety of percutaneous active mechanical support system (MCS) vs. control [intra-aortic balloon pumping (IABP)] in cardiogenic shock (CS). The primary endpoint of 30-day mortality and device-related complications including bleeding and leg ischemia were analyzed. Mean differences (MD) were calculated for mean arterial pressure (MAP), cardiac index (CI), pulmonary capillary wedge pressure (PCWP), and arterial lactate. Four trials randomizing 148 patients to either TandemHeart or Impella MCS (n=77) vs. control (n=71) were identified. Two trials used the TandemHeart device (Thiele et al. 2005; Burkhoff et al. 2006) and two trials used the Impella device [Impella 2.5 (Seyfarth, et al., 2008) and Impella CP (Ouweneel, et al., 2017)]. There was no difference in 30-day mortality. Active MCS significantly increased MAP and decreased arterial lactate at comparable CI and PCWP. No significant difference was observed in the incidence of leg ischemia whereas the rate of bleeding was significantly increased in MCS compared to IABP. The authors stated that despite an initial beneficial effect on MAP and arterial lactate active percutaneous MCS did not improve mortality in comparison to control in patients with CS complicating AMI. This may be partly explained by an excess of complications such as bleeding. The authors recommend that the use of active percutaneous MCS may thus be restricted to selected patients.

Cheng et al. (2009) conducted a meta-analysis of controlled trials to evaluate potential benefits of percutaneous LVADs on hemodynamics and thirty-day survival. Three trials met the inclusion criteria. Two of these evaluated the TandemHeart (Thiele et al. 2005; Burkhoff et al. 2006) and the third trial evaluated the Impella (Seyfarth, et al., 2008). These trials are described above. Weighted mean differences were calculated for cardiac index (CI), mean arterial pressure (MAP), and pulmonary capillary wedge pressure (PCWP). Relative risks were calculated for thirty-day mortality, leg ischemia, bleeding, and sepsis. After implantation, percutaneous LVAD patients had higher CI, higher MAP, and lower PCWP, compared with IABP patients. Similar thirty-day mortality was observed in both groups. No significant difference was seen in incidence of leg ischemia. Bleeding was significantly higher in TandemHeart patients compared to IABP patients. The authors stated that although percutaneous VADs provide superior hemodynamic support in patients with cardiogenic shock compared with IABP, the use of these devices did not improve early survival, and these results do not yet support percutaneous LVAD as a first-choice approach in the mechanical management of cardiogenic shock.

High-Risk PCI or Cardiogenic Shock: Shah et al. (2012) conducted a prospective observational study to evaluate the temporary use of a percutaneous left ventricular assist device (PLVAD) in 75 consecutive patients undergoing high-risk PCI or in cardiogenic shock. Patients undergoing high-risk PCI (n=57) and those in cardiogenic shock (n=17) were analyzed in separate cohorts. Patients undergoing PCI with intra-aortic balloon pump (IABP) (n=35) were compared to patients undergoing PCI with PLVAD (i.e., TandemHeart or Impella device) (n=22). Patients in cardiogenic shock treated with IABP (n=13) were compared to those treated with PLVAD (n=4). The primary endpoint was in-hospital major adverse cardiovascular events (MACE) and the secondary end point was in-hospital vascular complications. The primary and secondary endpoints were similar between groups for both high-risk PCI and cardiogenic shock. Patients presenting with ST elevated MI (STEMI) had IABP-assisted PCI more frequently, suggesting the speed of required support was important, and that infarct artery revascularization combined with IABP use adequately improved hemodynamics. The percentage of patients undergoing unprotected left main PCI and the number

of lesions treated were higher in the PLVAD group. This suggests that the operator chose PLVAD support more frequently for elective, complex PCI when extensive revascularization was required. Although several risk scores were higher in the PLVAD group, other risk scores were similar between groups. The authors stated that these findings suggest overall similar baseline risk between the groups. It is possible, however, that more extensive revascularization was achieved despite impaired left ventricular function with PLVAD support.

Meta-Analysis Cardiogenic Shock or High-Risk PCI: Rios et al. (2018) conducted a meta-analysis and Trial Sequential Analysis (TSA) comparing the benefits and harms of intra-aortic balloon pump (IABP) versus percutaneous ventricular assist devices (pVAD) (TandemHeart and the Impella 2.5, CP or 5.0) during high-risk percutaneous coronary intervention (PCI) or cardiogenic shock (CS). The authors included five randomized controlled trials (RCTs) (Thiele, et al., 2005 [n=20]; Burkhoff, et al., 2006 [n=35]; Seyfarth, et al., 2008 [n=32]; O'Neill, et al., 2012 [n=236]; Ouweneel, et al., 2017 [n=48]) and one nonrandomized study comparing pVAD versus IABP. Based on the RCTs, there was no difference in short-term (six months) (p=0.59) or long-term (12 months) (p=1.00) all-cause mortality. The use of pVAD seemed associated with more adverse events (acute kidney injury, limb ischemia, infection, major bleeding, and vascular injury) compared with IABP (p=0.008) but this was not supported by TSA (p=0.11). The authors concluded that further RCTs without bias and larger sample size are needed to establish more conclusively the role of these modalities of mechanical circulatory support during high-risk PCI or CS.

Acute Heart Failure: The RECOVER RIGHT pivotal study, a prospective, multi-center, non-randomized study, was the basis for the FDA HDE approval of the Impella RP System. The primary objective for the study was to assess safety and effectiveness of the use of the Impella RP device in patients (n=30) with right ventricular failure (RVF) refractory to medical treatment who require hemodynamic support. Inclusion criteria were patients who have developed signs of RVF either within 48 hours post-implantation of an FDA approved implantable surgical LVAD (Cohort A) or subsequent to post-cardiotomy cardiogenic shock within 48 hours post-surgery or post myocardial infarction (Cohort B). Eighteen subjects (60%) were enrolled in Cohort A and 12 subjects (40%) were enrolled in Cohort B. The primary endpoint of survival at 30 days or discharge post device removal (whichever is longer), or to induction of anesthesia for the next longer-term therapy was achieved in 73% of the study population, with 83% in cohort A and 58% in cohort B. The secondary safety endpoint was determined by the rates of the following adverse events at 30 days or discharge (whichever is longer), or at induction of anesthesia for a longer term therapy, including heart transplant or implant of a surgical RVAD (as a bridge-to-recovery or bridge-to-transplant): death (any cause of death and cardiac death); major bleeding; hemolysis; pulmonary embolism; tricuspid/pulmonary valve dysfunction (defined as tricuspid/pulmonic valve injury resulting in increased valve regurgitation versus baseline). The summary overall conclusions state that the RECOVER RIGHT was the first study of a percutaneous RVAD in patients with RVF refractory to medical treatment who had very limited therapeutic options. In the studied patient population, the use of the Impella RP device provided adequate circulatory support to reverse shock and to restore normal hemodynamic parameters, and achieved an overall survival rate of 73% at 30 days or discharge (whichever is longer) or to a long term therapy. The Impella RP device had a reasonable overall safety profile, with reliable percutaneous insertion and a low incidence of bleeding and vascular complications (Anderson, et al., 2015).

Bridge to Transplantation in Adults: The Impella 5.5 with SmartAssist system has been proposed for use as a bridge to transplantation in adults with end-stage heart failure. Literature is limited to a single case series reporting on outcomes in four individuals who all underwent successful heart transplantation after 81, 79, 65, and 54 days of Impella support. The study reported that one individual experienced 2 separate episodes of acute left posterior cerebral artery infarct on days 30 and 62 of support. There is insufficient evidence in the peer reviewed published

literature to support the safety and efficacy of percutaneous VADs as a bridge to transplantation in adults with end stage heart failure (Zaky, et al., 2023).

Implantable Aortic Counterpulsation Ventricular Assist Devices (VADs)

Permanently implantable aortic counterpulsation ventricular assist devices have been proposed as a bridge to recovery for patients with acute or chronic heart failure. These devices employ a counterpulsation device that is surgically implanted in the aorta, which inflates during diastole to reduce end diastolic ventricular pressure on a long-term basis without re-routing blood flow. Multiple devices are being investigated but presently no device has received FDA-approval. Examples of devices in development or in clinical trials include, but may not be limited to, the following: CardioVAD (LVAD Technology, Detroit, MI), Symphony device (Abiomed Inc, Danvers, MA), and the C-Pulse device (CHF Solutions Inc, Eden Prairie, MN) (Kontogiannis, et al., 2016; Gafoor, et al., 2015). There are scarce data in the published, peer-reviewed scientific literature regarding the safety and effectiveness of implantable aortic counterpulsation VADs in the treatment of heart failure.

Total Artificial Heart

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. 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 (Bartoli, 2011; Copeland, et al., 2004).

U.S. Food and Drug Administration (FDA)

SynCardia temporary Total Artificial Heart (SynCardia Systems, Inc., Tucson, AZ): The SynCardia temporary Total Artificial Heart (TAH-t) (P030011), 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.

The SynCardia Freedom® Driver System received FDA approval as a supplement to the original PMA on June 26, 2014 (P030011/S020). The device as modified is marketed under the trade name SynCardia temporary Total Artificial Heart with the Freedom Driver System and is indicated for use as a bridge to transplantation in cardiac transplant candidates who have been implanted with the temporary Total Artificial Heart (TAH-t) and are clinically stable. As with conventional hospital-based pneumatic drivers systems, the Freedom driver connects to the implanted TAH by a flexible pneumatic driveline that enters the body through the skin in the left chest below the ribs. It is powered by two onboard batteries which can be recharged using a standard electrical outlet or car charger. The Freedom Driver has been in use in Europe since 2010.

Literature Review

SynCardia temporary Total Artificial Heart (TAH): Nguyen et al. (2017) retrospectively analyzed the demographics, clinical characteristics and survival of 13 adult patients receiving the TAH. The patients received the TAH for refractory cardiogenic shock secondary to idiopathic (56%) or ischemic (17%) cardiomyopathy and to other various causes (33%). Before implantation, mean ejection fraction was 14% ± 4%, 7 (54%) patients had previous cardiac surgery, 4 (31%) were on mechanical ventilation, and 3 (23%) patients were on dialysis. According to the institutional policy, patients were not allowed to be discharged home with a portable console when these became available in Canada in 2011. The mean duration of TAH support was 46 ± 40 days. Three (23%) patients died while on support after a mean of 15 days. Actuarial survival on support was 77% ± 12% at 30 days after implantation. Complications on support included one stroke, acute respiratory distress syndrome requiring prolonged intubation (n=5 and acute renal failure requiring temporary dialysis (n=5). Ten (77%) patients survived to be transplanted after a mean of 52 ± 42 days of support. Actuarial survival rates after transplant were 67% ± 16% at one month and 56% ± 17% at 1 year after transplantation.

Demondion et al. (2013) conducted a retrospective analysis of clinical and biological data of 27 patients implanted with a Cardiowest (Syncardia) TAH between December 2006 and July 2010 at a single center in France. Fifteen patients (55.5%) died during device support; fourteen between implantation and discharge from intensive care, and one before home discharge. The major cause of death before discharge was multi-organ failure. Twelve (44.4%) patients left the hospital with a Freedom™ or Excor™ portable driver within a median of 88 days (range 35-152) post-implantation. The mean rehospitali-zation rate was 1.2 per patient, due to device infection (n=7), technical problems with the console (n=3) and other causes (n=4). Between implantation and transplant, patients spent 87% of their support time outside the hospital. All patients who were discharged home with the TAH were subsequently transplanted. One died post-transplant.

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 support, 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 inclusion criteria included: eligible for transplantation (according to institutional criteria) New York Heart Association class IV; body-surface area 1.7 to 2.5 m^2 or a distance of ≥10 cm from the anterior vertebral body to inner table of the sternum at 10th thoracic vertebra on computed tomographic scanning; hemodynamic

insufficiency according to either of the following definitions: Cardiac index ≤2.0 liters/min/$m^2$and one of the following: systolic arterial pressure ≤90 mm Hg or central venous pressure ≥18 mm Hg. Two of the following: dopamine at a dose of ≥10 µg/kg of body weight/min, dobutamine at a dose of ≥10 µg/kg/min, epinephrine at a dose of ≥2 µg/kg/min, other cardioactive drugs at maximal doses, use of an intraaortic balloon pump, or use of cardiopulmonary bypass. Exclusion criteria included: use of any vascular assist device; pulmonary vascular resistance ≥640 dyn · sec · cm^{-5} ;dialysis in previous 7 days; serum creatinine ≥5 mg/dl (440 µmol/liter); cirrhosis with total bilirubin ≥5 mg/dl (29 µmol/liter); cytotoxic antibody ≥10 percent. 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).

Professional Societies/Organizations
In a guidance document for mechanical circulatory support (MCS), the American Association for Thoracic Surgery/International Society for Heart and Lung Transplantation (Kirklin, et al., 2020) gave the following recommendations for MCS techniques in cardiogenic shock:

- "IABP support is recommended for cardiogenic shock complicating acute myocardial infarction, but additional mechanical support may be needed if prompt hemodynamic improvement is not forthcoming.
- Percutaneous LV to aorta pumps of appropriate size should be considered for cardiogenic shock from primary LV failure.
- Percutaneous right ventricular assist device support should be considered for cardiogenic shock from primary right ventricular failure."

The guidance document also gave the following recommendations for the use of biventricular support:

- "The possibility of biventricular support should be included in the surgical plan if biventricular failure is documented with CI<2.0 L/min/m2, right atrial pressure>17 mm Hg, and CVP/PCWP ratio>0.63.

- Patients who undergo placement of temporary MCS (percutaneous VAD or ECMO) should have right ventricle function evaluated at regular intervals; if it remains poor and patient is a transplant candidate, consideration for biventricular support or TAH is advisable.
- Patients who received an LVAD as bridge to transplant and remain with poorly controlled right ventricular failure (with or without a temporary right VAD) should be considered for longer-term biventricular support or TAH before end-organ dysfunction ensues."

The Society for Cardiovascular Angiography and Interventions (SCAI), Heart Failure Society of America (HFSA), Society of Thoracic Surgeons (STS), American Heart Association (AHA), and American College of Cardiology (ACC) "2015 Clinical Expert Consensus Statement on the Use of Percutaneous Mechanical Circulatory Support Devices in Cardiovascular Care" states that the availability of percutaneous mechanical circulatory support (MCS) has broadened therapeutic options for patients that require hemodynamic support. A variety of devices are now available, each with specific technical and clinical nuances. Definitive clinical evidence is in many cases either unavailable or controversial.

The following consensus-based summary statements are based upon the anticipated hemodynamic effects and risks, clinical outcomes data as well as knowledge gap:

- "Percutaneous MCS provides superior hemodynamic support compared to pharmacologic therapy. This is particularly apparent for the Impella and Tandem-Heart devices. These devices should remain available clinically and be appropriately reimbursed.
- Patients in cardiogenic shock represent an extremely high risk group in whom mortality has remained high despite revascularization and pharmacologic therapies. Early placement of an appropriate MCS may be considered in those who fail to stabilize or show signs of improvement quickly after initial interventions.
- MCS may be considered for patients undergoing high-risk PCI, such as those requiring multi-vessel, left main, or last patent conduit interventions, particularly if the patient is inoperable or has severely decreased ejection fraction or elevated cardiac filling pressures.
- In the setting of profound cardiogenic shock, IABP is less likely to provide benefit than continuous flow pumps including the Impella CP and TandemHeart. ECMO may also provide benefit, particularly for patients with impaired respiratory gas exchange.
- Patients with acute decompensated heart failure may benefit from early use of percutaneous MCS when they continue to deteriorate despite initial interventions. MCS may be considered if patients are candidates for surgically implanted VADs or if rapid recovery is expected (e.g., fulminant myocarditis or stress-induced cardiomyopathy).
- When oxygenation remains impaired, adding an oxygenator to a TandemHeart circuit or use of ECMO should be considered based upon local availability.
- There are insufficient data to support or refute the notion that routine use of MCSs as an adjunct to primary revascularization in the setting of large acute myocardial infarction is useful in reducing reperfusion injury or infarct size. Exploratory studies are underway.
- MCSs may be used for failure to wean off cardiopulmonary bypass, considered as an adjunct to high-risk electrophysiologic procedures when prolonged hypotension is anticipated, or rarely, for valvular interventions.
- Severe biventricular failure may require use of both right- and left-sided percutaneous MCS or venoarterial ECMO. Certain patients may respond to LVAD implantation with inotropes and/or pulmonary vasodilators to support the right heart. MCS may also be considered for isolated acute RVF complicated by cardiogenic shock.
- Registries and randomized controlled trials comparing different strategies in different clinical scenarios are critically needed (Rihal, et al., 2015)."

Heart Failure: The American Heart Association, American College of Cardiology, and Heart Failure Society of America 2022 clinical practice guideline for the management of heart failure states that mechanical circulatory support (MCS) is an option for patients with advanced heart failure with reduced ejection fraction (HFrEF) to prolong life and improve functional capacity. The guideline includes the following recommendations for the use of MCS:

- "In select patients with advanced HFrEF with NYHA class IV symptoms who are deemed to be dependent on continuous intravenous inotropes or temporary MCS, durable LVAD implantation is effective to improve functional status, quality of life, and survival. (Class 1 (strong) recommendation; Level A (high) quality of evidence)
- In select patients with advanced HFrEF who have NYHA class IV symptoms despite guideline-directed medical therapy (GDMT), durable MCS can be beneficial to improve symptoms, improve functional class, and reduce mortality (Class 2a (moderate) recommendation; Level B-R (moderate) quality of evidence)."
- "In patients with advanced HFrEF and hemodynamic compromise and shock, temporary MCS, including percutaneous and extracorporeal ventricular assist devices, are reasonable as a "bridge to recovery" or "bridge to decision (Class 2a (moderate) recommendation; Level B-NR (moderate) quality of evidence) (Heidenreich, et al., 2022)."

The Heart Failure Society of America (HFSA) published the following recommendation in the 2010 Comprehensive Heart Failure Practice Guideline:

- "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.
- Permanent mechanical assistance using an implantable assist device may be considered in highly selected patients with severe HF refractory to conventional therapy who are not candidates for heart transplantation, particularly those who cannot be weaned from intravenous inotropic support at an experienced HF center (Lindenfeld, et al., 2010)."

ST-Elevation MI (STEMI): The American College of Cardiology Foundation/American Heart Association (ACCF/AHA) "2013 Guidelines for the Management of ST-Elevation Myocardial Infarction" (O'Gara et al., 2013) include the following recommendations relevant to mechanical support in treatment of cardiogenic shock:

- "Alternative left ventricular (LV) assist devices for circulatory support may be considered in patients with refractory cardiogenic shock."

In a statement on the use of mechanical circulatory support, the American Heart Association indicated that some patients are too profoundly ill with multisystem organ failure to benefit from the best MCS and aggressive inotropic therapy and that complex decisions about candidacy for transplantation or MCS are best made by an experienced multidisciplinary team. While it may become appropriate for smaller programs to implant elective destination therapy MCS in highly selected patients, more acutely ill patients should be referred to quaternary care hospitals that are accustomed to the management of such patients.

The statement makes reference to MCS that may be used as a first step when rapid support is necessary in patients with cardiogenic shock who are at too high a risk for implantation of a durable (i.e., long-term) device, or as an alternative if recovery is possible. In the latter scenario, a bridge with a nondurable (i.e., temporary) MCS device provides stabilization and permits clarification and potential reversal of other medical issues thet may interfere with a satisfactory outcome after transplantation or long-term device placement. The following are included in a list of nondurable MCS devices that may be used as a bridge to recovery and for temporary support

until more definitive therapies can be used in patients in whom myocardial recovery does not occur: intra-aortic balloon pump (IABP), extracorporeal membrane oxygenation (ECMO), BVS 5000, AB5000, Thoratec pVAD, CentriMag, TandemHeart, and Impella. The statement also suggests that nondurable MCS may be used to determine neurological recovery or to stabilize potentially reversible comorbidities in patients with cardiogenic shock and potential candidates for transplantation.

The scientific statement includes the following recommendations:

- "MCS for bridge to transplant (BTT) indication should be considered for transplant-eligible patients with end-stage heart failure (HF) who are failing optimal medical, surgical, and/or device therapies and at high risk of dying before receiving a heart transplantation.
- Implantation of MCS in patients before the development of advanced HF (i.e., hyponatremia, hypotension, renal dysfunction, and recurrent hospitalizations) is associated with better outcomes. Therefore, early referral of advanced HF patients is reasonable.
- MCS with a durable, implantable device for permanent therapy or destination therapy (DT) is beneficial for patients with advanced HF, high 1-year mortality resulting from HF, and the absence of other life-limiting organ dysfunction; who are failing medical, surgical, and/or device therapies; and who are ineligible for heart transplantation.
- Elective rather than urgent implantation of destination therapy (DT) can be beneficial when performed after optimization of medical therapy in advanced HF patients who are failing medical, surgical, and/or device therapies.
- Urgent nondurable MCS is reasonable in hemodynamically compromised HF patients with end organ dysfunction and/or relative contraindications to heart transplantation/durable MCS that are expected to improve with time and restoration of an improved hemodynamic profile.
- Patients who are ineligible for heart transplantation because of pulmonary hypertension related to HF alone should be considered for bridge to potential transplant eligibility with durable, long-term MCS.
- Long-term MCS is not recommended in patients with advanced kidney disease in whom renal function is unlikely to recover despite improved hemodynamics and who are therefore at high risk for progression to renal replacement therapy. Long-term MCS as a bridge to heart–kidney transplantation might be considered on the basis of availability of outpatient hemodialysis (Peura, et al., 2012)."

Percutaneous Coronary Intervention: The American College of Cardiology Foundation/American Heart Association/Society for Cardiovascular Angiography and Intervention (ACCF/AHA/SCAI) "Guideline for Percutaneous Coronary Intervention" (Levine et al., 2011) includes the following recommendation:

- "Elective insertion of an appropriate hemodynamic support device as an adjunct to PCI may be reasonable in carefully selected high-risk patients."

High risk patients may include those undergoing unprotected left main or last-remaining-conduit PCI, those with severely depressed ejection fraction patients undergoing PCI of a vessel supplying a large territory, and/or those with cardiogenic shock. The guideline summarizes the limited evidence available on the use of percutaneous VADs, and states that patient risk, hemodynamic support, ease of application/removal, and operator and laboratory expertise are all factors involved in consideration of use of these devices. With devices that require large cannula insertion, the risk of vascular injury and related complications are important considerations regarding necessity and choice of device.

The following recommendation is given regarding cardiogenic shock:

- "A hemodynamic support device is recommended for patients with cardiogenic shock after STEMI who do not quickly stabilize with pharmacological therapy."

The guideline addresses procedural considerations for PCI in patients with cardiogenic shock, including pharmacological therapies, endotracheal intubation and mechanical ventilation with positive end-expiratory pressure for patients with respiratory failure, placement of a temporary pacemaker for patients with bradycardia or high-degree atrioventricular heart block, and use of a pulmonary artery catheter to provide information to dose and titrate inotropes and pressures. The authors also state, "Further hemodynamic support is available with IABP counterpulsation or percutaneous LV assist devices, although no data support a reduction in mortality rates."

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	Ventricular Assist Devices (20.9.1)	10/30/2013
NCD	National	Artificial Hearts and Related Devices (20.9)	10/30/2013
LCD		No Local Coverage Determination found	

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

Coding Information

Notes:

1. This list of codes may not be all-inclusive since the American Medical Association (AMA) and Centers for Medicare and Medicaid Services (CMS) code updates may occur more frequently than policy updates.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Implantable Ventricular Assist Devices (VADs)

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
33975	Insertion of ventricular assist device; extracorporeal, single ventricle
33976	Insertion of ventricular assist device; extracorporeal, biventricular
33979	Insertion of ventricular assist device, implantable, intracorporeal, single ventricle
33981	Replacement of extracorporeal ventricular assist device, single or biventricular, pump(s), single or each pump
33982	Replacement of ventricular assist device pump(s); implantable intracorporeal, single ventricle, without cardiopulmonary bypass
33983	Replacement of ventricular assist device pump(s); implantable intracorporeal, single ventricle, with cardiopulmonary bypass

HCPCS Codes	Description

Percutaneous Ventricular Assist Devices (VADs)

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
33990	Insertion of ventricular assist device, percutaneous including radiological supervision and interpretation; left heart, arterial access only
33991	Insertion of ventricular assist device, percutaneous including radiological supervision and interpretation; left heart, both arterial and venous access, with transseptal puncture
33993	Repositioning of percutaneous right or left heart ventricular assist device with imaging guidance at separate and distinct session from insertion

Implantable Aortic Counterpulsation Ventricular Assist Devices (VADs)

Considered Experimental/Investigational/Unproven when used to report insertion or replacement of a permanently implantable aortic counterpulsation ventricular assist system, endovascular approach, and programming of sensing and therapeutic parameters; removal of permanently implantable aortic counterpulsation ventricular assist system; relocation of skin pocket with replacement of implanted aortic counterpulsation ventricular assist device, mechano-electrical skin interface and electrodes; repositioning of previously implanted aortic counterpulsation ventricular assist device; programming device evaluation (in person) with iterative adjustment of the implantable mechano-electrical skin interface and/or external driver; and/or interrogation device evaluation (in person) with analysis, review, and report:

CPT®* Codes	Description
33999	Unlisted procedure, cardiac surgery

Total Artificial Heart

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
33927	Implantation of a total replacement heart system (artificial heart) with recipient cardiectomy
33928	Removal and replacement of total replacement heart system (artificial heart)
33999†	Unlisted procedure, cardiac surgery

†**Note: Considered Medically Necessary when used to report revision or replacement of components only of a replacement heart system (artificial heart) and when criteria in the applicable policy statements listed above are met.**

HCPCS Codes	Description
L8698††	Miscellaneous component, supply or accessory for use with total artificial heart system

††**Note: Considered Medically Necessary when used to report a component, supply, or accessory for use with a total artificial heart system and when criteria in the applicable policy statements listed above are met.**

Considered Medically Necessary when used to report the SynCardia Freedom® Driver System:

HCPCS Codes	Description
E1399	Durable medical equipment, miscellaneous

***Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.**

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Revision Details

Type of Revision	Summary of Changes	Date
Focused Review/Annual Review	• Added a not medically necessary policy statement for the SynCardia Freedom Driver System.	1/15/2025
Annual Review	• Changed contraindication verbiage from "malignancy that is expected to significantly limit future survival" to "incurable systemic malignancy". • Removed "a pattern of demonstrated noncompliance… which would place a VAD at serious risk of failure" from the list of contraindications. • Reorganized policy statements for percutaneous VADs. • Removed the statement pertaining to VADs used as part of an ECMO circuit from the policy statements. • Removed the SynCardia Freedom Driver System from the experimental,	12/15/2023

	investigational or unproven for any other indication policy statement.	