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MEDICAL POLICY – 7.03.09

Heart Transplant

BCBSA Ref. Policy:	7.03.09	
Effective Date:	Nov. 1, 2024	RELATED MEDICAL POLICIES:
Last Revised:	Oct. 7, 2024	7.03.08 Heart/Lung Transplant
		7.03.11 Total Artificial Hearts and Implantable Ventricular Assist Devices
Replaces:	Extracted from 7.03.509	

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | DOCUMENTATION REQUIREMENTS | CODING
RELATED INFORMATION | EVIDENCE REVIEW | REFERENCES | HISTORY

∞ Clicking this icon returns you to the hyperlinks menu above.

Introduction

An organ transplant is the surgical process of replacing a severely diseased organ with a healthy one from a donor. The donated organ can come from a living person or a person who passed away from an accident or illness. Organ failure is the most common reason a transplant is needed. Organ failure can occur because of illness, injury, or birth defect. There are many factors that go into finding a donor organ that matches. These include blood type and the size of the organ. Other factors include how long a person has been on the waiting list, the level of illness, and the distance the donated organ must be transported. This policy describes when transplanting a human heart may be considered medically necessary. This policy notes that a plan physician will review solid organ transplant requests together with the criteria of the transplant center.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Transplant	Medical Necessity

Human heart transplantation	**Human heart transplantation may be considered medically necessary for select adults and children with end-stage heart failure when the following individual selection criteria are met:**
	• Adult Individuals
	  ○ Accepted Indications for Cardiac Transplantation
	  ▪ Hemodynamic compromise due to heart failure demonstrated by any of the following 3 bulleted items:
	  ▫ Maximal oxygen consumption (VO_2) <10 mL/kg/min with achievement of anaerobic metabolism;
	  ▫ Refractory cardiogenic shock;
	  ▫ Documented dependence on intravenous inotropic support to maintain adequate organ perfusion;
	  OR
	  ▪ Severe ischemia consistently limiting routine activity not amenable to bypass surgery or angioplasty; or
	  ▪ Recurrent symptomatic ventricular arrhythmias refractory to all accepted therapeutic modalities
	  ○ Probable Indications for Cardiac Transplantation
	  ▪ Maximal VO_2 <14 mL/kg/min and major limitation of the individual's activities; or
	  ▪ Recurrent unstable ischemia not amenable to bypass surgery or angioplasty; or
	  ▪ Instability of fluid balance/renal function not due to individual noncompliance with a regimen of weight monitoring, flexible use of diuretic drugs, and salt restriction
	  ○ The following conditions are inadequate indications for cardiac transplantation unless other factors as listed above are present:
	  ▪ Ejection fraction <20%;
	  ▪ History of functional class III or IV symptoms of heart failure;
	  ▪ Previous ventricular arrhythmias;

Transplant	Medical Necessity
	▪ Maximal VO_2 >15 mL/kg/min • Pediatric Individuals ○ Individuals with heart failure and persistent symptoms at rest who require one or more of the following: ▪ Continuous infusion of intravenous inotropic agents; or ▪ Mechanical ventilatory support; or ▪ Mechanical circulatory support ○ Individuals with heart disease and symptoms of heart failure who do not meet the above criteria but who have any of the following: ▪ Severe limitation of exercise and activity (if measurable, such individuals would have a maximum VO_2 <50% predicted for age and sex); or ▪ Cardiomyopathies or previously repaired or palliated congenital heart disease and significant growth failure attributable to the heart disease; or ▪ Near sudden death and/or life-threatening arrhythmias untreatable with medications or an implantable defibrillator; or ▪ Restrictive cardiomyopathy with reactive pulmonary hypertension; or ▪ Reactive pulmonary hypertension and risk of developing fixed, irreversible elevation of pulmonary vascular resistance that could preclude orthotopic heart transplantation in the future; or ▪ Anatomic and physiologic conditions likely to worsen the natural history of congenital heart disease in infants with a functional single ventricle; or ▪ Anatomic and physiologic conditions that may lead to consideration for heart transplantation without systemic ventricular dysfunction
Heart retransplantation	**Heart retransplantation after a failed primary heart transplant may be considered medically necessary in individuals who meet the criteria for heart transplantation noted above.**

Transplant	Investigational
Heart transplantation	**Heart transplantation is considered investigational in all other situations not outlined above.**

Documentation Requirements
The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following: • Office visit notes that contain the relevant history and physical documenting the individual's end-stage heart failure and the specific condition from the list above indicating the individual meets the medical necessity criteria for a heart transplantation or retransplantation.

Coding

Code	Description
CPT	
33945	Heart transplant, with or without recipient cardiectomy
HCPCS	
S2152	Solid organ(s), complete or segmental, single organ or combination of organs; deceased or living donor (s), procurement, transplantation, and related complications; including: drugs; supplies; hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services, and the number of days of pre and posttransplant care in the global definition

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

New York Heart Association (NYHA) Classification	
Class I	No symptoms and no limitation in ordinary physical activity, e.g., shortness of breath when walking, climbing stairs etc.
Class II	Mild symptoms (mild shortness of breath and/or angina) and slight limitation during ordinary activity

New York Heart Association (NYHA) Classification	
Class III	Marked limitation in activity due to symptoms, even during less-than-ordinary activity, e.g., walking short distances (20–100 m). Comfortable only at rest.
Class IV	Severe limitations. Experiences symptoms even while at rest. Mostly bedbound patients

Cardiac-Specific Criteria

Specific criteria for prioritizing donor thoracic organs for transplant are provided by the Organ Procurement and Transplantation Network (OPTN) and implemented through a contract with United Network for Organ Sharing (UNOS). Donor thoracic organs are prioritized by UNOS on the basis of recipient medical urgency, distance from donor hospital, and pediatric status. Individuals who are most severely ill (status 1A) are given the highest priority. The following factors are considered in assessing the severity of illness: reliance on continuous mechanical ventilation, infusion of intravenous inotropes, and/or dependency on mechanical circulatory support (i.e., total artificial heart, intra-aortic balloon pump, extracorporeal membrane oxygenator, ventricular assist device).

Additional criteria, which are considered in pediatric individuals, include diagnosis of an OPTN-approved congenital heart disease, presence of ductal dependent pulmonary or systemic circulation, and diagnosis of hypertrophic or restrictive cardiomyopathy while less than one year old. Of note, pediatric heart transplant candidates who remain on the waiting list at the time of their 18th birthday without receiving a transplant continue to qualify for medical urgency status based on the pediatric criteria.

Specific criteria for prioritizing donor thoracic organs for retransplant include severe coronary allograft vasculopathy, mild or moderate coronary allograft vasculopathy with a left ventricular ejection fraction less than 45%, coronary allograft vasculopathy with restrictive physiology, or symptomatic graft dysfunction without evidence of active rejection.

Contraindications

Potential contraindications for solid organ transplant are subject to the judgment of the transplant center include the following:

- Known current malignancy, including metastatic cancer
- Recent malignancy with high risk of recurrence

- Untreated systemic infection making immunosuppression unsafe, including chronic infection
- Other irreversible end-stage diseases not attributed to heart or lung disease
- History of cancer with a moderate risk of recurrence
- Systemic disease that could be exacerbated by immunosuppression
- Psychosocial conditions or chemical dependency affecting ability to adhere to therapy.

Policy-specific potential contraindications include:

- Pulmonary hypertension that is fixed as evidenced by pulmonary vascular resistance >5 Wood units, or transpulmonary gradient ≥16 mm/Hg despite treatment[a]
- Severe pulmonary disease, despite optimal medical therapy, not expected to improve with heart transplantation[a]

Note: [a] Some individuals may be candidates for combined heart and lung transplantation (see **Related Policies**).

Individuals must meet the UNOS guidelines for status 1A, 1B, or status 2 (and not currently be status 7).

Benefit Application

See individual's plan contract language for organ transplant benefits and specific benefits related to transport, lodging, and donor services. Please note limitations in coverage based on the transplant benefit, if applicable.

Evidence Review

Description

A heart transplant and a retransplant consists of replacing a diseased heart with a healthy donor heart. Transplantation is used for individuals with refractory end-stage cardiac disease.

Background

Solid Organ Transplantation

Solid organ transplantation offers a treatment option for individuals with different types of end-stage organ failure that can be lifesaving or provide significant improvements to an individual's quality of life.[1] Many advances have been made in the last several decades to reduce perioperative complications. Available data support improvement in long-term survival as well as improved quality of life, particularly for liver, kidney, pancreas, heart, and lung transplants. Allograft rejection remains a key early and late complication risk for any organ transplantation. Transplant recipients require life-long immunosuppression to prevent rejection. Individuals are prioritized for transplant by mortality risk and severity of illness criteria developed by the Organ Procurement and Transplantation Network and United Network for Organ Sharing (UNOS).

Heart Transplant

In 2023, 46,632 transplants were performed in the United States (US) procured from 39,679 deceased donors and 6,953 living donors.[2] Heart transplants were the third most common procedure with 4,039 transplants performed from both deceased and living donors in 2023. As of June 2024 , there were 3,440 patients on the waiting list for a heart transplant.[3] Rose et al (2024) reported a 62% lower rate of heart transplants among women compared with men and a 46% lower rate in Black men compared with White men in a retrospective database review from 2010 to 2018.[4]

Most heart transplant recipients now are hospitalized as status 1 individuals at the time of transplant. This shift has occurred due to the increasing demand for the scarce resource of donor organs resulting in an increased waiting time for recipients. Individuals initially listed as status 2 candidates may deteriorate to a status 1 candidate before a donor organ becomes available. Alternatively, as medical and device therapy for advanced heart failure improves, some individuals on the transplant list will recover enough function to be delisted. Lietz and Miller (2007) reported on survival for individuals on the heart transplant waiting list, comparing the era between 1990 and 1994 with the era of 2000 to 2005.[5] One-year survival for a UNOS status 1 candidate improved from 49.5% to 69.0%. Status 2 candidates fared even better, with 89.4% surviving 1 year compared with 81.8% in the earlier time period.

Johnson et al (2010) reported on waiting list trends in the US between 1999 and 2008.[6] The proportion of individuals listed as status 1 increased, even as the waiting list and posttransplant mortality for this group have decreased. Meanwhile, status 2 individuals have decreased as a

proportion of all candidates. Completed transplants have trended toward the extremes of age, with more infants and individuals older than age 65 years having transplants in recent years. Bakhtiyar et al (2020) evaluated survival among individuals (N=95,323) wait-listed for heart transplantation between January 1, 1987, and December 29, 2017, using UNOS data.[7] Results revealed one year survival on the wait list increased from 34.1% in 1987 to 1990 to 67.8% in 2011 to 2017 (difference in proportions, 0.34%; 95% confidence interval [CI], 0.32% to 0.36%; *P*<.001). One year wait list survival also significantly increased for candidates with ventricular assist devices from 10.2% in 1996 to 2000 to 70% in 2011 to 2017 (difference in proportions, 0.60%; 95% CI, 0.58% to 0.62%; *P*<.001).

Alshawabkeh et al (2018) reported on the one year probability of the combined outcome of death or delisting due to clinical worsening for individuals on the heart transplant waiting list, comparing the periods of April 1, 1986 to January 19, 1999, (early era) and January 20, 1999 to June 2, 2014 (current era).[8] For adults without congenital heart disease (CHD), the probability of the combined outcome was lower in the current era compared with the early era, regardless of whether the individual was listed in status I (14.5% vs 22.7%; *P*<.0001) or 2 (9.0% vs 12.8%, *P*<0.0001). When comparing the current and early eras in adults with CHD, a reduction in the probability of the combined outcome was demonstrated in those listed in status I (17.6% vs 43.3%, respectively; *P*<.0001), whereas the outcome remained unchanged for those listed in status 2 (10.6% vs 10.4%, respectively; *P*=.94).

In adults with CHD, factors associated with waitlist death or delisting due to clinical worsening within 1 year were also examined by Alshawabkeh et al (2016).[9] A multivariate analysis identified that an estimated glomerular filtration rate less than 60 ml/min/1.73 m^2 (hazard ratio [HR], 1.4; 95% CI, 1.0 to 1.9; *P*=.043), albumin less than 3.2 g/dl (HR, 2.0; 95% CI, 1.3 to 2.9; *P*<.001), and hospitalization at the time of listing in the intensive care unit (HR, 2.3; 95% CI, 1.6 to 3.5; p<0.001) or a non-intensive care hospital unit (HR, 1.9; 95% CI, 1.2 to 3.0; *P*=.006) were associated with waitlist death or delisting due to clinical worsening within one year.

Magnetta et al (2019) reported outcomes for children on the heart transplant waiting list, comparing the periods of December 16, 2011 to March 21, 2016 (era 1), and March 22, 2016 to June 30, 2018 (era 2).[10] There was a significant decrease from era 1 to era 2 in the proportion of individuals listed as status 1 (70% vs 56%; *P*<.001), while the proportion of individuals with CHD significantly increased across eras (49% to 54%; *P*=.018). The median time on the waitlist increased from 68 days to 78 days (*P*=.005). There were no significant differences across eras in the cumulative incidence of death on the waitlist among all candidates (subdistribution HR, 0.96; 95% CI, 0.80 to 1.14; *P*=.63) and among those listed status 1A (subdistribution HR, 1.16; 95% CI, 0.95 to 1.41; *P*=.14). Graft survival at 90 days was also similar across eras in the overall population and in those with CHD (*P*>.53 for both).

As a consequence, aggressive treatment of heart failure has been emphasized in recent guidelines. Prognostic criteria have been investigated to identify individuals who have truly exhausted medical therapy and thus are likely to derive the maximum benefit for heart transplantation. Maximal oxygen consumption (VO_2max), which is measured during maximal exercise, is a measure suggested as a critical objective criterion of the functional reserve of the heart. The American College of Cardiology and American Heart Association have adopted VO_2max as a criterion for individual selection.[11]

Methods other than VO_2max have been proposed as predictive models in adults.[12,13,14,15] The Heart Failure Survival Scale and the Seattle Heart Failure Model (SHFM) are examples. In particular, the SHFM provides an estimate of one-, two-, and three-year survival with the use of routinely obtained clinical and laboratory data. Information on pharmacologic and device usage is incorporated into the model, permitting some estimation on the effects of current, more aggressive heart failure treatment strategies. Levy et al (2006) introduced the model using a multivariate analysis of data from the Prospective Randomized Amlodipine Survival Evaluation-1 heart failure trial (n=1125).[16] Applied to the data of five other heart failure trials, SHFM correlated well with actual survival (r=0.98). SHFM has been validated in both ambulatory and hospitalized heart failure populations,[17,18,19] but with a noted underestimation of mortality risk, particularly in Black adults and device recipients.[20,21] None of these models has been universally adopted by transplant centers.

Summary of Evidence

For individuals who have end-stage heart failure who receive a heart transplant, the evidence includes retrospective studies and registry data. The relevant outcomes are overall survival (OS), symptoms, and morbid events. Heart transplant remains a viable treatment for those with severe heart dysfunction despite appropriate medical management with medication, surgery, or medical devices. Given the exceedingly poor survival rates without transplantation for these individuals, evidence of post-transplant survival is sufficient to demonstrate that heart transplantation provides a survival benefit. Heart transplantation is contraindicated for individuals for whom the procedure is expected to be futile due to comorbid disease or for whom post-transplantation care is expected to worsen comorbid conditions significantly. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have had a prior heart transplant complicated by graft failure or severe dysfunction of the heart who receive a heart retransplant, the evidence includes systematic reviews, retrospective studies, and registry data. The relevant outcomes are OS, symptoms, and

morbid events. Despite improvements in the prognosis for many individuals with graft failure, cardiac allograft vasculopathy, and severe dysfunction of the transplanted heart, heart retransplant remains a viable treatment for those whose severe symptoms persist despite treatment with other medical or surgical remedies. Given the exceedingly poor survival rates without retransplantation for individuals who have exhausted other treatments, evidence of posttransplant survival is sufficient to demonstrate that heart retransplantation provides a survival benefit in appropriately selected individuals. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Ongoing and Unpublished Clinical Trials

A search of **ClinicalTrials.gov** in June 2024 did not identify any ongoing or unpublished trials that would likely influence this review.

Practice Guidelines and Position Statements

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the policy conclusions.

Guidelines or position statements will be considered for inclusion if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence. Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American College of Cardiology Foundation et al

Heart failure guidelines from the American College of Cardiology Foundation, the American Heart Association, and the Heart Failure Society of America were updated in 2022.[11]

Recommendations for cardiac transplantation by the joint committee were as follows:

- "For selected patients with advanced HF [heart failure] despite GDMT [guideline-directed medical therapy], cardiac transplantation is indicated to improve survival and QOL [quality of life] (class of recommendation, 1; level of evidence, C-LD)

- In patients with stage D (advanced) HF despite GDMT, cardiac transplantation provides intermediate economic value (value statement: intermediate value)"

International Society for Heart and Lung Transplantation

In 2004, the International Society for Heart and Lung Transplantation (ISHLT) recommended that children with the following conditions be evaluated for heart transplantation (see **Table 1**).[68]

Table 1. Recommendations for Pediatric Heart Transplant

Recommendation	LOE
Diastolic dysfunction that is refractory to optimal medical/surgical management because they are at high risk of developing pulmonary hypertension and of sudden death	B
Advanced systemic right ventricular failure (Heart Failure Stage C described as patients with underlying structural or functional heart disease and past or current symptoms of heart failure) that is refractory to medical therapy	C

LOE B is based on a single randomized trial or multiple nonrandomized trials; LOE C is based primarily on expert consensus opinion.
LOE: level of evidence.

In 2016 the ISHLT published a 10-year update to its listing criteria for heart transplantation.[69] The guidelines recommended the following updates or changes to the prior guideline:

- Recommended use of heart failure prognosis scores (e.g., Seattle Heart Failure Model, Heart Failure Survival Score) along with a cardiopulmonary exercise test to determine prognosis and guide listing for transplantation for ambulatory patients.
- Periodic right heart catheterization for routine surveillance was not recommended in children.
- Carefully selected patients >70 years of age may be considered for cardiac transplantation.
- Pre-existing neoplasm, body mass index of ≥35 kg/m^2, diabetes with "end-organ damage (other than non-proliferative retinopathy) or poor glycemic control … despite optimal effort," irreversible renal dysfunction, clinically severe symptomatic cerebrovascular disease, peripheral vascular disease, and frailty are considered relative contraindications to heart transplantation.

- Considering active smoking during the previous 6 months as a risk factor for poor outcomes after transplantation, active tobacco smoking is considered a relative contraindication for heart transplantation. Similarly, patients who remain active substance abusers (including alcohol) are not recommended to receive heart transplantation.

In 2016 this same ISHLT guideline update states the following regarding retransplantation indications:

"Retransplantation is indicated for those patients who develop significant CAV [(cardiac allograft vasculopathy)] with refractory cardiac allograph dysfunction, without evidence of ongoing acute rejection (Class IIa, Level of Evidence: C)."

The guideline cites the published consensus by Johnson et al (2007) on indications for retransplantation.[6] It states that based on available data, appropriate indications for retransplantation include "the development of chronic severe CAV with symptoms of ischemia or heart failure, CAV without symptoms but with moderate to severe LV [(left ventricle)] dysfunction, or symptomatic graft dysfunction without evidence of active rejection." Retransplantation within the first six months after previous transplantation, especially with immunologic complications as a primary cause, was considered high-risk.

As a note on heart transplantation in children, the 2016 guideline update states, "although nearly half of all HTs [(heart transplants)] in children are done for CHD [(congenital heart disease)],… it should be noted that general considerations vary for more traditional indications, such as idiopathic dilated cardiomyopathy, for transplantation in the pediatric population…Thus, as these guidelines are translated to the younger patient, such prudence will need to be exercised."

In 2010, the guidelines from ISHLT on the care of heart transplant recipients include the following recommendations on cardiac retransplantation[70]:

- "Retransplantation is indicated in children with at least moderate systolic heart allograft dysfunction and/or severe diastolic dysfunction and at least moderate CAV (cardiac allograft vasculopathy)."
- "It is reasonable to consider listing for retransplantation those adult HT [heart transplant] recipients who develop severe CAV not amenable to medical or surgical therapy and symptoms of heart failure or ischemia."
- "It is reasonable to consider listing for retransplantation those HT recipients with heart allograft dysfunction and symptomatic heart failure occurring in the absence of acute rejection."

- "It is reasonable to consider retransplantation in children with normal heart allograft function and severe CAV."

American Heart Association

In 2007, the American Heart Association indicated that, based on level B (nonrandomized studies) or level C (consensus opinion of experts) evidence, heart transplantation is indicated for pediatric individuals as therapy for the following indications: [67]

- Stage D heart failure (interpreted as abnormal cardiac structure and/or function, continuous infusion of intravenous inotropes, or prostaglandin E_1 to maintain patency of a ductus arteriosus, mechanical ventilatory and/or mechanical circulatory support) associated with systemic ventricular dysfunction in patients with cardiomyopathies or previous repaired or palliated congenital heart disease,
- Stage C heart failure (interpreted as abnormal cardiac structure and/or function and past or present symptoms of heart failure) associated with pediatric heart disease and severe limitation of exercise and activity, in patients with cardiomyopathies or previously repaired or palliated congenital heart disease and heart failure associated with significant growth failure attributed to heart disease, pediatric heart disease with associated near sudden death and/or life-threatening arrhythmias untreatable with medications or an implantable defibrillator, or in pediatric restrictive cardiomyopathy disease associated with reactive pulmonary hypertension;

The guideline states that heart transplantation is feasible in the presence of other indications for heart transplantation, "in patients with pediatric heart disease and an elevated pulmonary vascular resistance index >6 Woods units/m^2 and/or a transpulmonary pressure gradient >15 mm Hg if administration of inotropic support or pulmonary vasodilators can decrease pulmonary vascular resistance to <6 Woods units/m^2 or the transpulmonary gradient to <15 mm Hg."

Medicare National Coverage

Cardiac transplantation is covered under Medicare when performed in a facility approved by Medicare.[71] The Centers for Medicare & Medicaid Services has stated that, under certain limited cases, exceptions to the criteria may be warranted if there is justification and if the facility ensures safety and efficacy objectives.

Regulatory Status

Solid organ transplants are a surgical procedure and, as such, are not subject to regulation by the US Food and Drug Administration (FDA).

The FDA regulates human cells and tissues intended for implantation, transplantation, or infusion through the Center for Biologics Evaluation and Research, under Code of Federal Regulation Title 21, parts 1270 and 1271. Solid organs used for transplantation are subject to these regulations.

References

1. Black CK, Termanini KM, Aguirre O, et al. Solid organ transplantation in the 21 st century. Ann Transl Med. Oct 2018; 6(20): 409. PMID 30498736
2. United Network for Organ Sharing (UNOS). Data and trends. 2024; **https://unos.org/data/transplant-trends/**. Accessed Sept. 4, 2024.
3. Organ Procurement and Transplantation Network (OPTN). National data. 2024; **https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/**. Accessed Sept. 4, 2024.
4. Rose SW, Strackman BW, Gilbert ON, et al. Disparities by Sex, Race, and Ethnicity in Use of Left Ventricular Assist Devices and Heart Transplants Among Patients With Heart Failure With Reduced Ejection Fraction. J Am Heart Assoc. Jan 16 2024; 13(2): e031021. PMID 38166429
5. Lietz K, Miller LW. Improved survival of patients with end-stage heart failure listed for heart transplantation: analysis of organ procurement and transplantation network/U.S. United Network of Organ Sharing data, 1990 to 2005. J Am Coll Cardiol. Sep 25 2007; 50(13): 1282-90. PMID 17888847
6. Johnson MR, Meyer KH, Haft J, et al. Heart transplantation in the United States, 1999-2008. Am J Transplant. Apr 2010; 10(4 Pt 2): 1035-46. PMID 20420651
7. Bakhtiyar SS, Godfrey EL, Ahmed S, et al. Survival on the Heart Transplant Waiting List. JAMA Cardiol. Nov 01 2020; 5(11): 1227-1235. PMID 32785619
8. Alshawabkeh L, Opotowsky AR, Carter KD, et al. Disparities in Wait-List Outcomes for Adults With Congenital Heart Disease Listed for Heart Transplantation Before and Since Revision of Status I Listing. Am J Cardiol. Nov 15 2018; 122(10): 1761-1764. PMID 30236623
9. Alshawabkeh LI, Hu N, Carter KD, et al. Wait-List Outcomes for Adults With Congenital Heart Disease Listed for Heart Transplantation in the U.S. J Am Coll Cardiol. Aug 30 2016; 68(9): 908-17. PMID 27561764
10. Magnetta DA, Godown J, West S, et al. Impact of the 2016 revision of US Pediatric Heart Allocation Policy on waitlist characteristics and outcomes. Am J Transplant. Dec 2019; 19(12): 3276-3283. PMID 31544351
11. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. May 03 2022; 79(17): e263-e421. PMID 35379503

12. Aaronson KD, Schwartz JS, Chen TM, et al. Development and prospective validation of a clinical index to predict survival in ambulatory patients referred for cardiac transplant evaluation. Circulation. Jun 17 1997; 95(12): 2660-7. PMID 9193435

13. Alla F, Briançon S, Juillière Y, et al. Differential clinical prognostic classifications in dilated and ischemic advanced heart failure: the EPICAL study. Am Heart J. May 2000; 139(5): 895-904. PMID 10783225

14. Hansen A, Haass M, Zugck C, et al. Prognostic value of Doppler echocardiographic mitral inflow patterns: implications for risk stratification in patients with chronic congestive heart failure. J Am Coll Cardiol. Mar 15 2001; 37(4): 1049-55. PMID 11263607

15. Lee DS, Austin PC, Rouleau JL, et al. Predicting mortality among patients hospitalized for heart failure: derivation and validation of a clinical model. JAMA. Nov 19 2003; 290(19): 2581-7. PMID 14625335

16. Levy WC, Mozaffarian D, Linker DT, et al. The Seattle Heart Failure Model: prediction of survival in heart failure. Circulation. Mar 21 2006; 113(11): 1424-33. PMID 16534009

17. Gorodeski EZ, Chu EC, Chow CH, et al. Application of the Seattle Heart Failure Model in ambulatory patients presented to an advanced heart failure therapeutics committee. Circ Heart Fail. Nov 2010; 3(6): 706-14. PMID 20798278

18. Ketchum ES, Moorman AJ, Fishbein DP, et al. Predictive value of the Seattle Heart Failure Model in patients undergoing left ventricular assist device placement. J Heart Lung Transplant. Sep 2010; 29(9): 1021-5. PMID 20558086

19. Nutter AL, Tanawuttiwat T, Silver MA. Evaluation of 6 prognostic models used to calculate mortality rates in elderly heart failure patients with a fatal heart failure admission. Congest Heart Fail. 2010; 16(5): 196-201. PMID 20887615

20. Kalogeropoulos AP, Georgiopoulou VV, Giamouzis G, et al. Utility of the Seattle Heart Failure Model in patients with advanced heart failure. J Am Coll Cardiol. Jan 27 2009; 53(4): 334-42. PMID 19161882

21. May HT, Horne BD, Levy WC, et al. Validation of the Seattle Heart Failure Model in a community-based heart failure population and enhancement by adding B-type natriuretic peptide. Am J Cardiol. Aug 15 2007; 100(4): 697-700. PMID 17697831

22. Virani SS, Alonso A, Aparicio HJ, et al. Heart Disease and Stroke Statistics-2021 Update: A Report From the American Heart Association. Circulation. Feb 23 2021; 143(8): e254-e743. PMID 33501848

23. Lund LH, Edwards LB, Dipchand AI, et al. The Registry of the International Society for Heart and Lung Transplantation: Thirty-third Adult Heart Transplantation Report-2016; Focus Theme: Primary Diagnostic Indications for Transplant. J Heart Lung Transplant. Oct 2016; 35(10): 1158-1169. PMID 27772668

24. Jaramillo N, Segovia J, Gomez-Bueno M, et al. Characteristics of patients with survival longer than 20 years following heart transplantation. Rev Esp Cardiol. Oct 2013;66(10):797-802. PMID 23932221

25. Nguyen VP, Mahr C, Mokadam NA, et al. The Benefit of Donor-Recipient Matching for Patients Undergoing Heart Transplantation. J Am Coll Cardiol. Apr 04 2017; 69(13): 1707-1714. PMID 28359517

26. Rana A, Gruessner A, Agopian VG, et al. Survival benefit of solid-organ transplant in the United States. JAMA Surg. Mar 01 2015; 150(3): 252-9. PMID 25629390

27. Kilic A, Weiss ES, George TJ, et al. What predicts long-term survival after heart transplantation? An analysis of 9,400 ten-year survivors. Ann Thorac Surg. Mar 2012; 93(3): 699-704. PMID 22226494

28. Dipchand AI, Kirk R, Mahle WT, et al. Ten yr of pediatric heart transplantation: a report from the Pediatric Heart Transplant Study. Pediatr Transplant. Mar 2013; 17(2): 99-111. PMID 23442098

29. Auerbach SR, Richmond ME, Chen JM, et al. Multiple risk factors before pediatric cardiac transplantation are associated with increased graft loss. Pediatr Cardiol. Jan 2012; 33(1): 49-54. PMID 21892650

30. Rossano JW, Dipchand AI, Edwards LB, et al. The Registry of the International Society for Heart and Lung Transplantation: Nineteenth Pediatric Heart Transplantation Report-2016; Focus Theme: Primary Diagnostic Indications for Transplant. J Heart Lung Transplant. Oct 2016; 35(10): 1185-1195. PMID 27772670

31. Savla J, Lin KY, Lefkowitz DS, et al. Adolescent age and heart transplantation outcomes in myocarditis or congenital heart disease. J Heart Lung Transplant. Sep 2014; 33(9): 943-9. PMID 24929645

32. Almond CSD, Thiagarajan RR, Piercey GE, et al. Waiting list mortality among children listed for heart transplantation in the United States. Circulation. Feb 10 2009; 119(5): 717-727. PMID 19171850

33. Tjang YS, Tenderich G, Hornik L, et al. Cardiac retransplantation in adults: an evidence-based systematic review. Thorac Cardiovasc Surg. Sep 2008; 56(6): 323-7. PMID 18704853

34. Zhu Y, Shudo Y, Lingala B, et al. Outcomes after heart retransplantation: A 50-year single-center experience. J Thorac Cardiovasc Surg. Feb 2022; 163(2): 712-720.e6. PMID 32798029

35. Saito A, Novick RJ, Kiaii B, et al. Early and late outcomes after cardiac retransplantation. Can J Surg. Feb 2013; 56(1): 21-6. PMID 23187039

36. Miller RJH, Clarke BA, Howlett JG, et al. Outcomes in patients undergoing cardiac retransplantation: A propensity matched cohort analysis of the UNOS Registry. J Heart Lung Transplant. Oct 2019; 38(10): 1067-1074. PMID 31378576

37. Goldraich LA, Stehlik J, Kucheryavaya AY, et al. Retransplant and Medical Therapy for Cardiac Allograft Vasculopathy: International Society for Heart and Lung Transplantation Registry Analysis. Am J Transplant. Jan 2016; 16(1): 301-9. PMID 26274617

38. Belli E, Leoni Moreno JC, Hosenpud J, et al. Preoperative risk factors predict survival following cardiac retransplantation: analysis of the United Network for Organ Sharing database. J Thorac Cardiovasc Surg. Jun 2014; 147(6): 1972-7, 1977.e1. PMID 24636155

39. Friedland-Little JM, Gajarski RJ, Yu S, et al. Outcomes of third heart transplants in pediatric and young adult patients: analysis of the United Network for Organ Sharing database. J Heart Lung Transplant. Sep 2014; 33(9): 917-23. PMID 24861821

40. Bock MJ, Nguyen K, Malerba S, et al. Pediatric cardiac retransplantation: Waitlist mortality stratified by age and era. J Heart Lung Transplant. Apr 2015; 34(4): 530-7. PMID 25016920

41. Conway J, Manlhiot C, Kirk R, et al. Mortality and morbidity after retransplantation after primary heart transplant in childhood: an analysis from the registry of the International Society for Heart and Lung Transplantation. J Heart Lung Transplant. Mar 2014; 33(3): 241-51. PMID 24462559

42. Mistiaen WP. Heart transplantation in patients with previous malignancy. An overview. Acta Cardiol. Apr 2015; 70(2): 123-30. PMID 26148371

43. Yoosabai A, Mehta A, Kang W, et al. Pretransplant malignancy as a risk factor for posttransplant malignancy after heart transplantation. Transplantation. Feb 2015; 99(2): 345-50. PMID 25606783

44. Oliveira GH, Hardaway BW, Kucheryavaya AY, et al. Characteristics and survival of patients with chemotherapy-induced cardiomyopathy undergoing heart transplantation. J Heart Lung Transplant. Aug 2012; 31(8): 805-10. PMID 22551930

45. Sigurdardottir V, Bjortuft O, Eiskjær H, et al. Long-term follow-up of lung and heart transplant recipients with pre-transplant malignancies. J Heart Lung Transplant. Dec 2012; 31(12): 1276-80. PMID 23089300

46. Agüero F, Castel MA, Cocchi S, et al. An Update on Heart Transplantation in Human Immunodeficiency Virus-Infected Patients. Am J Transplant. Jan 2016; 16(1): 21-8. PMID 26523614

47. Uriel N, Jorde UP, Cotarlan V, et al. Heart transplantation in human immunodeficiency virus-positive patients. J Heart Lung Transplant. Jul 2009; 28(7): 667-9. PMID 19560693

48. Doberne JW, Jawitz OK, Raman V, et al. Heart Transplantation Survival Outcomes of HIV Positive and Negative Recipients. Ann Thorac Surg. May 2021; 111(5): 1465-1471. PMID 32946847

49. Organ Procurement and Transplantation Network (OPTN). Organ Procurement and Transplantation Network Policies. 2024; **https://optn.transplant.hrsa.gov/governance/policies/**. Accessed Sept. 4, 2024.

50. Working Party of the British Transplantation Society. Kidney and Pancreas Transplantation in Patients with HIV. Second Edition (Revised). British Transplantation Society Guidelines. Macclesfield, UK: British Transplantation Society; 2017.

51. Jamil A, Qin H, Felius J, et al. Comparison of Clinical Characteristics, Complications, and Outcomes in Recipients Having Heart Transplants 65 Years of Age Versus ≥65 Years of Age. Am J Cardiol. Dec 15 2017; 120(12): 2207-2212. PMID 29056228

52. Cooper LB, Lu D, Mentz RJ, et al. Cardiac transplantation for older patients: Characteristics and outcomes in the septuagenarian population. J Heart Lung Transplant. Mar 2016; 35(3): 362-369. PMID 26632028

53. Awad M, Czer LS, Mirocha J, et al. Similar Mortality and Morbidity of Orthotopic Heart Transplantation for Patients 70 Years of Age and Older Compared With Younger Patients. Transplant Proc. Oct 2016; 48(8): 2782-2791. PMID 27788818

54. Kilic A, Weiss ES, Yuh DD, et al. Factors associated with 5-year survival in older heart transplant recipients. J Thorac Cardiovasc Surg. Feb 2012; 143(2): 468-74. PMID 22248684

55. De Santo LS, Romano G, Maiello C, et al. Pulmonary artery hypertension in heart transplant recipients: how much is too much?. Eur J Cardiothorac Surg. Nov 2012; 42(5): 864-9; discussion 869-70. PMID 22402452

56. Perez-Villa F, Farrero M, Cardona M, et al. Bosentan in heart transplantation candidates with severe pulmonary hypertension: efficacy, safety and outcome after transplantation. Clin Transplant. 2013; 27(1): 25-31. PMID 22861120

57. Pons J, Leblanc MH, Bernier M, et al. Effects of chronic sildenafil use on pulmonary hemodynamics and clinical outcomes in heart transplantation. J Heart Lung Transplant. Dec 2012; 31(12): 1281-7. PMID 23127754

58. Bedanova H, Orban M, Vrsansky D, et al. Impact of pulmonary hypertension on early hemodynamics, morbidity and mortality after orthotopic heart transplantation. A single center study. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. Mar 2013; 157(1): 35-40. PMID 23073529

59. Tsukashita M, Takayama H, Takeda K, et al. Effect of pulmonary vascular resistance before left ventricular assist device implantation on short- and long-term post-transplant survival. J Thorac Cardiovasc Surg. Nov 2015; 150(5): 1352-60, 1361.e1-2. PMID 26253875

60. Arshad A, Kew EP, Lim S. Comparison of Renal Outcomes in Patients With Left Ventricular Assist Device and Heart Transplantation. Transplant Proc. Dec 2019; 51(10): 3395-3398. PMID 31810507

61. Kolsrud O, Karason K, Holmberg E, et al. Renal function and outcome after heart transplantation. J Thorac Cardiovasc Surg. Apr 2018; 155(4): 1593-1604.e1. PMID 29338859

62. Hong KN, Merlo A, Chauhan D, et al. Evidence supports severe renal insufficiency as a relative contraindication to heart transplantation. J Heart Lung Transplant. Jul 2016; 35(7): 893-900. PMID 27105687

63. Goel AN, Iyengar A, Schowengerdt K, et al. Heart transplantation in children with intellectual disability: An analysis of the UNOS database. Pediatr Transplant. Mar 2017; 21(2). PMID 27933693

64. Wightman A, Bartlett HL, Zhao Q, et al. Prevalence and outcomes of heart transplantation in children with intellectual disability. Pediatr Transplant. Mar 2017; 21(2). PMID 27801533

65. Wightman A, Bradford MC, Hsu E, et al. Prevalence and Long-Term Outcomes of Solid Organ Transplant in Children with Intellectual Disability. J Pediatr. Aug 2021; 235: 10-17.e4. PMID 33794218

66. Prendergast C, McKane M, Dodd DA, et al. The impact of cognitive delay on pediatric heart transplant outcomes. Pediatr Transplant. Mar 2017; 21(2). PMID 28191755

67. Canter CE, Shaddy RE, Bernstein D, et al. Indications for heart transplantation in pediatric heart disease: a scientific statement from the American Heart Association Council on Cardiovascular Disease in the Young; the Councils on Clinical Cardiology, Cardiovascular Nursing, and Cardiovascular Surgery and Anesthesia; and the Quality of Care and Outcomes Research Interdisciplinary Working Group. Circulation. Feb 06 2007; 115(5): 658-76. PMID 17261651

68. Rosenthal D, Chrisant MR, Edens E, et al. International Society for Heart and Lung Transplantation: Practice guidelines for management of heart failure in children. J Heart Lung Transplant. Dec 2004; 23(12): 1313-33. PMID 15607659

69. Mehra MR, Canter CE, Hannan MM, et al. The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: A 10-year update. J Heart Lung Transplant. Jan 2016; 35(1): 1-23. PMID 26776864

70. Costanzo MR, Dipchand A, Starling R, et al. The International Society of Heart and Lung Transplantation Guidelines for the care of heart transplant recipients. J Heart Lung Transplant. Aug 2010; 29(8): 914-56. PMID 20643330

71. Centers for Medicare & Medicaid Services (CMS). National Coverage Determination (NCD) for HEART TRANSPLANTs (260.9). 2008; **NCD - Heart Transplants (260.9) (cms.gov)**. Accessed Sept. 4, 2024.

History

Date	Comments
11/01/19	New policy, approved October 4, 2019. Content previously addressed in policy 7.03.509. Policy created with literature review through June 2019. Heart transplantation may be considered medically necessary when criteria are met. Policy statement on transplantation of HCV viremic organs is taken from BCBSA policy 7.03.14.
04/01/20	Delete policy, approved March 10, 2020. This policy will be deleted effective July 2, 2020, and replaced with InterQual criteria for dates of service on or after July 2, 2020.
05/06/20	Interim Review, approved May 5, 2020. This policy is reinstated immediately and will no longer be deleted or replaced with InterQual criteria on July 2, 2020.
11/01/20	Annual Review, approved October 22, 2020. Policy updated with literature review through June 2020; references added. Policy statements unchanged.
11/01/21	Annual Review, approved October 5, 2021. Policy updated with literature review through June 16, 2021; references added. Policy statements unchanged.
11/01/22	Annual Review, approved October 10, 2022. Policy updated with literature review through June 10, 2022; reference added. Minor editorial refinements to policy statements; intent unchanged. Changed the wording from "patient" to "individual" throughout the policy for standardization.
11/01/23	Annual Review, approved October 9, 2023. Policy updated with literature review through June 28, 2023; reference added. Removed the policy statement regarding the transplantation of HCV-viremic solid organs to an HCV non-viremic recipient combined with direct-acting antiviral treatment for HCV is considered investigational. Otherwise, policy statements unchanged.
11/01/24	Annual Review, approved October 7, 2024. Policy updated with literature review through June 21, 2024; reference added. Policy statements unchanged.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.