

(70309)

Medical Benefit	Effective Date: 04/01/14	Next Review Date: 01/18
Preauthorization	Yes	Review Dates: 01/10, 01/11, 01/12, 01/13, 01/14, 01/15, 01/16, 01/17

Preauthorization is required and must be obtained through Case Management.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none"> • With end-stage heart failure 	Interventions of interest are: <ul style="list-style-type: none"> • Heart transplant 	Comparators of interest are: <ul style="list-style-type: none"> • Medical management • Cardiac device-based management (e.g., left ventricular assist device, total artificial heart) 	Relevant outcomes include: <ul style="list-style-type: none"> • Overall survival • Symptoms • Morbid events • Treatment-related mortality • Treatment-related morbidity

Description

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

Summary of Evidence

The evidence for the use of heart transplant in patients who have end-stage heart failure includes case series and registry data. Relevant outcomes are overall survival, symptoms, morbid events, and treatment-related morbidity and mortality. Despite an improvement in prognosis for many patients with advanced heart disease, heart transplant remains a viable treatment for those who have exhausted other medical or surgical remedies, yet are still in end-stage disease. Given the exceedingly poor survival without transplantation of patients who have exhausted other treatments, evidence of posttransplant survival is sufficient to demonstrate that heart transplantation provides a survival benefit in appropriately selected patients. Heart transplantation is contraindicated in patients in whom the procedure is expected to be futile due to comorbid disease or in whom post-transplantation care is expected to significantly worsen comorbid conditions. Similarly, evidence suggests that heart retransplantation after a failed primary heart transplant provides a survival benefit in patients who still meet criteria for heart transplantation and do not have contraindications.

Policy

Human heart transplantation may be considered **medically necessary** for selected adults and children with end-stage heart failure when patient selection criteria are met.

Adult Patients

I. Accepted Indications for Transplantation

1. Hemodynamic compromise due to heart failure demonstrated by any of the following three bulleted items,
 - Maximal VO_2 (oxygen consumption) less than 10 mL/kg/min with achievement of anaerobic metabolism
 - Refractory cardiogenic shock
 - Documented dependence on intravenous inotropic support to maintain adequate organ perfusion, or
2. Severe ischemia consistently limiting routine activity not amenable to bypass surgery or angioplasty, or
3. Recurrent symptomatic ventricular arrhythmias refractory to ALL accepted therapeutic modalities.

II. Probable Indications for Cardiac Transplantation

1. Maximal VO_2 less than 14 mL/kg/min and major limitation of the patient's activities, or
2. Recurrent unstable ischemia not amenable to bypass surgery or angioplasty, or
3. Instability of fluid balance/renal function not due to patient noncompliance with regimen of weight monitoring, flexible use of diuretic drugs, and salt restriction.

III. The following conditions are inadequate indications for transplantation unless other factors as listed above are present:

1. Ejection fraction less than 20%
2. History of functional class III or IV symptoms of heart failure
3. Previous ventricular arrhythmias
4. Maximal VO_2 greater than 15 mL/kg/min.

Pediatric Patients

1. Patients with heart failure with 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.
2. Patients with pediatric heart disease with symptoms of heart failure who do not meet the above criteria but who have:
 - Severe limitation of exercise and activity (if measurable, such patients would have a peak maximum oxygen consumption less than 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 potential risk of developing fixed, irreversible elevation of pulmonary vascular resistance that could preclude orthotopic heart transplantation in the future; or
- Anatomical and physiological conditions likely to worsen the natural history of congenital heart disease in infants with a functional single ventricle; or
- Anatomical and physiological conditions that may lead to consideration for heart transplantation without systemic ventricular dysfunction.

Heart retransplantation after a failed primary heart transplant may be considered **medically necessary** in patients who meet criteria for heart transplantation.

Heart transplantation is considered **investigational** in all other situations.

Policy Guidelines

Individual transplant facilities may have their own additional requirements or protocols that must be met in order for the patient to be eligible for a transplant at their facility.

Potential contraindications subject to the judgment of the transplant center:

1. Known current malignancy, including metastatic cancer
2. Recent malignancy with high risk of recurrence
3. Untreated systemic infection making immunosuppression unsafe, including chronic infection
4. Other irreversible end-stage disease not attributed to heart or lung disease
5. History of cancer with a moderate risk of recurrence
6. Systemic disease that could be exacerbated by immunosuppression
7. Psychosocial conditions or chemical dependency affecting ability to adhere to therapy

Policy-specific potential contraindications

1. Pulmonary hypertension that is fixed as evidenced by pulmonary vascular resistance (PVR) greater than five Wood units, or trans-pulmonary gradient (TPG) greater than or equal to 16 mm/Hg despite treatment*
2. Severe pulmonary disease despite optimal medical therapy, not expected to improve with heart transplantation.*

*Some patients may be candidates for combined heart-lung transplantation (See the Heart/Lung Transplant Protocol).

Patients must meet the United Network for Organ Sharing (UNOS) guidelines for 1A, 1B, or 2 Status and not currently be Status 7.

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 the 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. Patients who are most severely ill (Status IA) are given highest priority. Criteria from OPTN for listing status are as follows (Organ Procurement and Transplantation Network, 2015):

Adult patients (18 years of age or older)

STATUS 1A

A patient is admitted to the listing transplant center hospital and has at least one of the following devices or therapies in place:

1. Mechanical circulatory support that includes at least one of the following:
 - a) Total artificial heart
 - b) Intra-aortic balloon pump, or
 - c) Extracorporeal membrane oxygenator (ECMO)
2. Continuous mechanical ventilation
3. Requires continuous infusion of a single high-dose intravenous inotrope or multiple intravenous inotropes, and requires continuous hemodynamic monitoring of left ventricular filling pressures.

A patient has one of the following devices or therapies in place (with or without being admitted to the listing transplant center hospital):

1. Mechanical circulatory support that includes at least one of the following:
 - a) Left ventricular assist device (LVAD)
 - b) Right ventricular assist device (RVAD)
 - c) Left and right ventricular assist devices (BiVAD)
2. Mechanical circulatory support and there is medical evidence of significant device-related complications including, but not limited to, thromboembolism, device infection, mechanical failure, or life-threatening ventricular arrhythmias.

STATUS 1B

A patient has at least one of the following devices or therapies in place:

1. Left ventricular assist device (LVAD)
2. Right ventricular assist device (RVAD)
3. Left and right ventricular assist devices (BiVAD)
4. Continuous infusion of intravenous inotropes

A patient that does not meet Status 1A or 1B is listed as Status 2.

Pediatric patients

A candidate listed as Status 1A meets at least one of the following criteria:

1. Requires assistance with a mechanical ventilator;
2. Requires assistance with a mechanical assist device (e.g., ECMO);
3. Requires assistance with a balloon pump;
4. Is younger than six months old with congenital or acquired heart disease exhibiting reactive pulmonary hypertension at greater than 50% of systemic level. Such a candidate may be treated with prostaglandin E (PGE) to maintain patency of the ductus arteriosus;
5. Requires infusion of a single high dose of an intravenous inotrope or multiple intravenous inotropes or multiple inotropes (e.g., addition of dopamine at greater than or equal to 5.0 µg/kg/min); or

6. Has a life expectancy without a heart transplant of less than 14 days.

A candidate listed as Status 1B meets at least one of the following criteria:

1. Requires infusion of low dose single inotropes;
2. Is younger than six months old and does not meet the criteria for Status 1A; or
3. Is in the less than 5th percentile for the candidates expected height and/or weight according to most recent Centers for Disease Control and Prevention's (CDC) National Center for Health Statistics pediatric clinical growth chart;
4. Is 1.5 or more standard deviations below the candidate's expected height growth or weight growth according to the most recent CDC National Center for Health Statistics pediatric clinical growth chart.

A candidate who does not meet the criteria for Status 1A or 1B is listed as Status 2.

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 upon the pediatric criteria.

Status 7 patients are considered temporarily unsuitable to receive a thoracic organ transplant.

Medicare Advantage

If a transplant is needed, we arrange to have the Medicare-approved transplant center review and decide whether the patient is an appropriate candidate for the transplant.

Background

In the United States, approximately 5.8 million people have heart failure and 300,000 die each year from this condition.¹ The reduction of cardiac output is considered to be severe when systemic circulation cannot meet the body's needs under minimal exertion. Heart transplantation can potentially improve both survival and quality of life in patients with end-stage heart failure.

Heart failure may be due to a number of differing etiologies, including ischemic heart disease, cardiomyopathy, or congenital heart defects. The leading indication for heart transplant has shifted over time from ischemic to nonischemic cardiomyopathy. During the period 2005 to 2010, the primary causes of heart failure in patients undergoing transplant operations were nonischemic cardiomyopathy (53%) and ischemic cardiomyopathy (38%). Approximately 3% of the heart transplants during this time period were in adults with congenital heart disease.¹

The demand for heart transplants far exceeds the availability of donor organs, and the length of time patients are on the waiting list for transplants has increased. According to data from the Organ Procurement and Transplantation Network (OPTN), in 2014, a total of 2655 heart transplants were performed in the United States.² As of October 30, 2015, there were 4207 patients on the waiting list for a heart transplant. Also in recent years, advances in medical and device therapy for patients with advanced heart failure has improved the survival of patients awaiting heart transplantation. The chronic shortage of donor hearts has led to the prioritization of patients awaiting transplantation to ensure greater access for patients most likely to derive benefit. Prioritization criteria are issued by OPTN and fulfilled through a contract with the United Network for Organ Sharing.³

From 2005 to 2010, approximately 3% of heart transplants were repeat transplantations.¹ Heart retransplantation raises ethical issues due to the lack of sufficient donor hearts for initial transplants. UNOS does not have separate organ allocation criteria for repeat heart transplant recipients.

Regulatory Status

Heart transplantation is a surgical procedure and, as such, is not subject to regulation by the U.S. Food and Drug Administration (FDA).

Related Protocols

Heart/Lung Transplant

Immune Cell Function Assay

Laboratory Tests for Heart Transplant Rejection

Total Artificial Hearts and Implantable Ventricular Assist Devices

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

1. Fischer S, Glas KE. A review of cardiac transplantation. *Anesthesiol Clin*. Jun 2013; 31(2):383-403. PMID 23711649
2. Organ Procurement and Transplantation Network (OPTN). 2015; <http://optn.transplant.hrsa.gov/latestData/viewDataReports.asp>. Accessed November 4, 2015.
3. (OPTN) OPaTN. Organ Procurement and Transplantation Network: Policies (last updated November 2, 2015). 2015; http://optn.transplant.hrsa.gov/ContentDocuments/OPTN_Policies.pdf#nameddest=Policy_09. Accessed November 5, 2015.
4. Lietz K, Miller LW. Improved survival of patients with end-stage heart failure listed for heart transplantation analysis of organ procurement transplantation, network U. S. United Network of Organ Sharing data, 1990 to 2005. *J Am Coll Cardiol*. 2007; 50(13):1282-1290.
5. Johnson MR, Meyer KH, Haft J, et al. Heart transplantation in the United States, 1999-2008. *Am J Transplant*. 2010; 10(4 Pt 2):1035-1046.
6. Hunt SA, Abraham WT, Chin MH, et al. ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure): developed in collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Transplantation: endorsed by the Heart Rhythm Society. *Circulation*. 2005; 112(12):e154-235.

7. Costanzo MR, Augustine S, Bourge RS, et al. A statement for health professionals from the Committee on Heart Failure and Cardiac Transplantation of the Council on Clinical Cardiology, American Heart Association. *Circulation*. 1995; 92(12):3593-3612.
8. 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*. 1997; 95(12):2660-2667.
9. Alla F, Briancon S, Juilliere Y, et al. Differential clinical prognostic classifications in dilated and ischemic advanced heart failure: the EPICAL study. *Am Heart J*. 2000; 139(5):895-904.
10. 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*. 2001; 37(4):1049-1055.
11. Lee DS, Austin PC, Rouleau JL, et al. Predicting mortality among patients hospitalized for heart failure: derivation and validation of a clinical model. *Jama*. 2003; 290(19):2581-2587.
12. Levy WC, Mozaffarian D, Linker DT, et al. The Seattle Heart Failure Model: prediction of survival in heart failure. *Circulation*. 2006; 113(11):1424-1433.
13. Gorodeski E, Chu E, Chow C, et al. Application of the Seattle Heart Failure Model in Ambulatory Patients Presented to an Advanced Heart Failure Therapeutics Committee. *Circ Heart Fail* 2010; 3(6):706-714.
14. 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*. 2010; 29(9):1021-1025.
15. 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.
16. 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*. 2009; 53(4):334-342.
17. 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*. 2007; 100(4):697-700.
18. Rana A, Gruessner A, Agopian VG, et al. Survival benefit of solid-organ transplant in the United States. *JAMA Surg*. Mar 1 2015; 150(3):252-259. PMID 25629390
19. 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
20. 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
21. 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
22. 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):943-949. PMID 24929645
23. Kirk R, Dipchand AI, Edwards LB, et al. The registry of the international society for heart and lung transplantation: fifteenth pediatric heart transplantation report-2012. *J Heart Lung Transplant*. Oct 2012; 31(10):1065-1072. PMID 22975096
24. Almond CS, Thiagarajan RR, Piercey GE, et al. Waiting list mortality among children listed for heart transplantation in the United States. *Circulation*. 2009; 119(5):717-727.
25. 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
26. 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):1972-1977, 1977 e1971. PMID 24636155
27. Tjang YS, Tenderich G, Hornik L, et al. Cardiac retransplantation in adults: an evidence-based systematic review. *Thorac Cardiovasc Surg*. Sep 2008; 56(6):323-327. PMID 18704853

28. Saito A, Novick RJ, Kiaii B, et al. Early and late outcomes after cardiac retransplantation. *Can J Surg*. Feb 26. PMID 23187039
29. 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):917-923. PMID 24861821
30. Bock MJ, Nguyen K, Malerba S, et al. Pediatric cardiac retransplantation: Waitlist mortality stratified by age and era. *J Heart Lung Transplant*. Jun 4 2014. PMID 25016920
31. Mahle WT, Vincent RN, Kanter KR. Cardiac retransplantation in childhood: analysis of data from the United Network for Organ Sharing. *J Thorac Cardiovasc Surg*. Aug 2005; 130(2):542-546. PMID 16077425
32. Kasiske BL, Snyder JJ, Gilbertson DT, et al. Cancer after kidney transplantation in the United States. *Am J Transplant*. 2004; 4(6):905-913.
33. Taylor DO, Edwards LB, Boucek MM, et al. Registry of the International Society for Heart and Lung Transplantation: twenty-second official adult heart transplant report--2005. *J Heart Lung Transplant*. 2005; 24(8):945-955.
34. Otley CC, Hirose R, Salasche SJ. Skin cancer as a contraindication to organ transplantation. *Am J Transplant*. 2005; 5(9):2079-2084.
35. Trofe J, Buell JF, Woodle ES, et al. Recurrence risk after organ transplantation in patients with a history of Hodgkin disease or non-Hodgkin lymphoma. *Transplantation*. 2004; 78(7):972-977.
36. 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):345-350. PMID 25606783
37. Taylor DO, Farhoud HH, Kfoury G, et al. Cardiac transplantation in survivors of lymphoma: a multi-institutional survey. *Transplantation*. 2000; 69(10):2112-2115.
38. Uriel N, Jorde UP, Cotarlan V, et al. Heart transplantation in human immunodeficiency virus-positive patients. *J Heart Lung Transplant*. Jul 2009; 28(7):667-669. PMID 19560693
39. Organ Procurement and Transplantation Network. Policy Management. <http://optn.transplant.hrsa.gov/policiesAndBylaws/policies.asp>. Accessed August 22, 2014.
40. Bhagani S, Sweny P, Brook G. Guidelines for kidney transplantation in patients with HIV disease. *HIV Med*. 2006; 7(3):133-139.
41. Daneshvar D, Czer LS, Phan A, et al. Heart transplantation in patients aged 70 years and older: a two-decade experience. *Transplant Proc*. Dec 2011; 43(10):3851-3856. PMID 22172859
42. 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):468-474. PMID 22248684
43. 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):864-869; discussion 869-870. PMID 22402452
44. 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*. Jan-Feb 2013; 27(1):25-31. PMID 22861120
45. 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):1281-1287. PMID 23127754
46. 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
47. 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*. 2004; 23(12):1313-1333.
48. Kirk R, Dipchand AI, Rosenthal DN, et al. The International Society of Heart and Lung Transplantation Guidelines for the management of pediatric heart failure: Executive summary. *J Heart Lung Transplant*. Sep 2014; 33(9):888-909. PMID 25110323

49. Mehra MR, Kobashigawa J, Starling R, et al. Listing criteria for heart transplantation: International Society for Heart and Lung Transplantation guidelines for the care of cardiac transplant candidates--2006. *J Heart Lung Transplant*. Sep 2006; 25(9):1024-1042. PMID 16962464
50. 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):914-956. PMID 20643330
51. 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 6 2007; 115(5):658-676. PMID 17261651
52. Centers for Medicare and Medicaid Services (CMS). National Coverage Determination (NCD) for HEART TRANSPLANTS (260.9). <http://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=112&ncdver=3&CoverageSelection=National&Keyword=heart+transplant&KeywordLookup=Title&KeywordSearchType=And&clickon=search&bc=gAAAABAAAA&>. Accessed August 22, 2014.