Solid organ transplantation

Clinical guidelines

Effective Date: September 9, 2024

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Guideline Application

For medical necessity clinical coverage criteria for Medicare Advantage plans, refer first to the Medicare Coverage Database for NCDs and LCDs/LCAs, then the Medicare Benefit Policy Coverage Manual.

SARS-CoV-2-vaccination

Optum supports the recommendations of the American Society of Transplant Surgeons (ASTS), American Society of Transplantation (AST) and The International Society for Heart and Lung Transplantation (ISHLT) concerning vaccination against SARS-CoV-2. Optum encourages solid organ transplant candidates to discuss the following ASTS/AST/ISHLT recommendations of their transplant team:

- Solid organ transplant recipients should be vaccinated against SARS-CoV-2, using locally approved vaccines
- Eligible household and close contacts of solid organ transplant recipients should be vaccinated against SARS-CoV-2
- Whenever possible, vaccination should occur prior to transplantation, ideally with completion of vaccine series a minimum of 2 weeks prior to transplant.

Optum understands there are many additional issues relevant to the individual member such as local prevalence of SARS-CoV-2 and its variants, personal situations relating to immunosuppression and transplant infections, and the vaccination level in the household. Decisions concerning vaccination should be made by the member in consultation with the member's transplant team.

Reference

ASTS, AST, ISHLT Joint Statement about COVID-19 Vaccination in Organ Transplant Candidates and Recipients. Nov 29, 2021. ISHLT-AST-ASTS_Joint-Statement_COVID19-Vaccination_30-December.pdf.

Universal contraindications

NOTE: *The following list contains the standard contraindications for solid organ transplants. These contraindications apply to ALL types of transplants unless otherwise noted. There may be additional contraindications or exceptions that apply to a specific type of transplant. Please refer to the "Contraindications" section in the specific type of transplant for more information.*

- Infections:
  - Systemic or uncontrolled infection including sepsis
- Significant uncorrectable life-limiting medical conditions
- Severe end-stage organ damage that would have an impact on patient survival
- Active untreated or untreatable malignancy
- Irreversible, severe brain damage
- Active substance use disorders
  While there is no evidence-based, optimal period of sobriety, an attempt at a period of at least 90 days abstinence is expected. This would allow sufficient clinical improvement which may, in turn, avert the need for transplantation. *See the organ-specific transplant sections below for additional information.*
- Inactive alcohol and/or substance abuse (alcohol, crystal meth, heroin, cocaine, methadone, and/or narcotics, etc.) is not a contraindication
- Recreational or medicinal use of marijuana is not a contraindication

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Kidney including kidney/liver, kidney/heart, and kidney/lung

General Information

- For multi-organ transplant, patient must meet criteria for each organ.
- Kidney transplantation is the treatment of choice for suitable patients with end-stage kidney disease.
- Preemptive living donor transplantation is encouraged whenever possible.
- Candidates should be referred to a transplant center as soon as it appears probable that renal replacement therapy (dialysis) will be needed within the next 6–12 months (Kasiske et al., 2001).
- Due to the very long wait times and the likely increased burden of comorbid conditions, patients over the age of 70 may not be considered for deceased donor transplantation by many kidney transplant programs. In many instances, while a member 70–75 years of age may not be considered for a deceased donor transplant, a center may be willing to evaluate an older patient for a living donor transplant.
    - The importance of living donation in this situation should be emphasized with the patient.
- Wait times in many parts of the country can last for years, particularly for those with blood groups O and B and those who are highly sensitized. Strategies to increase the likelihood of getting an organ include:
    - Patients should be very strongly encouraged to consider living donation and to seek out potential donors. Kidney Paired Donation/Exchange (KPD) is considered medically necessary.
    - Double-listing in another United Network for Organ Sharing (UNOS) Region with a shorter wait time should be discussed and encouraged if the patient's living situation will allow the flexibility to do this.
    - ABO incompatible transplants are considered medically necessary.
    - Desensitization protocols for highly sensitized (high PRA/panel-reactive antibody) patients are considered medically necessary.
- Candidates should be informed that placement on the cadaveric waiting list does not guarantee transplantation, since changes in their medical status may delay or preclude transplantation (Kasiske et al., 2001).
    - If a patient will have to be on a waiting list for a long time, the importance of maintaining transplant readiness by strict adherence to all advice from the transplant center, the treating nephrologist and the dialysis center should be emphasized.
- Patients with primary oxalosis with ESRD should be considered for combined liver/kidney transplant (Eason et al., 2008; Compagnon et al., 2014).

Indications

- When to refer (Bunnapradist & Danovitch, 2007):
    - Kidney transplantation should be discussed with all patients with irreversible advanced chronic kidney disease (CKD).

    - Patients with CKD without known contraindications for transplantation should be referred to a transplant program when they approach CKD stage 4 or a glomerular filtration rate (GFR) less than 30 ml/min/1.73 m^2.
    - Early referral will improve the chances of a patient receiving a preemptive transplant, especially those with a potential living donor; referral to a kidney transplant program does not imply immediate transplantation.
- End-stage renal disease (ESRD):
    - Chronic renal failure with glomerular filtration rate (GFR) < 20ml/min
    - Chronic renal failure on dialysis
    - Symptomatic uremia
- Anticipated ESRD as defined above within next 12 months (preemptive transplantation).
- Combined kidney/liver transplant *when at least one* the following are present: (OPTN Policy 9.9 Liver-Kidney Allocation; Table 9-17 Medical Eligibility Criteria for Liver-Kidney Allocation). See Appendix A for National Kidney Foundation (NKF) definition of chronic kidney disease (CKD).
    - Candidates with sustained acute kidney injury (AKI):
        - Dialysis at least once every 7 days for the last 6 weeks

          AND/OR

        - eGFR ≤ 25 mL/min at least once every 7 days for the last 6 weeks
    - Candidates with chronic kidney disease (CKD) as defined by the National Kidney Foundation (NKF) **AND** at least one of the following:
        - Regularly administered dialysis as an end-stage renal disease (ESRD) patient in a hospital based, independent non-hospital based, or home setting
        - eGFR ≤ 30 mL/min at time of listing
    - Candidates diagnosed with at least one of the following:
        - Hyperoxaluria
        - Atypical hemolytic uremic syndrome (HUS) from mutations in factor H or factor I
        - Familial non-neuropathic systemic amyloidosis
        - Methylmalonic aciduria
- Simultaneous heart/kidney transplant:
    - See criteria in the heart transplantation section of the Guidelines.
- Retransplantation. Usually due to primary non-function, rejection, recurrent disease and/or immunosuppression toxicity.

Organ-specific contraindications

Please review the Universal Contraindications found at the beginning of the Guidelines. These apply to all transplants unless otherwise noted below. Additional contraindications that are specific to a particular type of transplant are noted below. Refer to the Medical Director.

- Reversible renal failure (Bunnapradist & Danovitch, 2007)

Considerations for substance use disorder

For patients experiencing catastrophic decompensation where a period of abstinence is not realistic the transplant center must have an institutional protocol that requires, at a minimum:

- Appropriate patient and psychosocial support profile. Transplant center must have an institutional protocol to conduct psychosocial evaluation and proactively implement interventions to promote post-transplant success.
    - Presence of close supportive social network

  - Absence of severe coexisting behavioral health disorders that would negatively impact a treatment plan
  - Agreement by patient (with support of his/her social network) to post-transplant rehabilitation and monitoring, and to lifelong abstinence from addictive substances
- Evaluation by addiction specialist indicating high likelihood of success of post-transplant rehabilitation and abstinence
- Approval by a transplant selection committee that includes in addition to the regular members, a psychiatrist and/or an addiction specialist
- No special consideration for acute decompensation with illicit drug addiction and/or abuse
- Any other substance abuse needs to be addressed
- Inactive alcohol and/or substance abuse (alcohol, crystal meth, heroin, cocaine, methadone, and/or narcotics, etc.) is not a contraindication

Special Considerations

Additional consultation and/or evaluation may be indicated in these situations. Refer to Medical Director if questions remain.

These recommendations are consistent with the 2001 American Society of Transplantation (AST) Clinical Practice Guidelines (Kasiske et al., 2001).

- Primary non-function or less than one year since the initial transplant may require additional evaluation to determine causative factors.
- Patients with a history of malignancy require an oncology evaluation to determine status of disease. Recommendations for suitability and timing of a solid organ transplant following successful treatment of malignancy may be found in Appendix B. The recommendations are based on Al-Adra et al. (2021).
- Social and psychiatric issues can have a significant impact on the outcomes of a transplant. It is expected that a psychosocial evaluation and/or psychiatry consultation is obtained as part of the standard transplant evaluation (Crone et al., 2010). The evaluation should address the following:
  - Overall functioning
  - Understanding of underlying illness and need for proposed treatment
  - History of adherence and compliance and barriers to compliance
  - Quality of relationships
  - Presence of a supportive caregiver
  - Social history, including educational level and employment history
  - Housing and living situation, including reliable transportation to attend medical visits
  - Socioeconomic status, including sufficient funding to pay for immunosuppressive medications post-transplant
  - Current and past history of alcohol and substance use and abuse
  - Current and past psychiatric history, including baseline cognitive status and coping skills
- Patients with human immunodeficiency virus (HIV) infection must be on a highly active antiretroviral therapy (HAART) regimen and there must be documented evidence of sustained viral load suppression.
- BMI ≥ 35 kg/m^2. NOTE: There are few data to suggest which, if any, obese patients should be denied transplantation based on obesity per se (Kasiske et al., 2001).
  - Refer to requesting program patient selection criteria.
  - If outside the program's patient selection criteria, refer to Medical Director.

- Pediatric patients should have a normal history and physical, or if there is any indication of abnormal cardiac function, cardiology evaluation should be obtained.
- Adult patients with known heart disease including, but not limited to, heart failure, cardiomyopathy and coronary artery disease require cardiology consultation and completion of consultant's recommendations, if any.
- Gastrointestinal (GI) clearance may be indicated in patients with a history of complicated or active GI disorders.
- Significant, uncorrectable pulmonary disease. Pulmonary consultation and completion of consultant's recommendations if any is required.

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Liver

General Information

Patients may be placed on the UNOS waiting list for liver transplantation for a variety of reasons; hence, the overall clinical status will determine the need for listing. However, priority status is currently defined by the Model for End-Stage Liver Disease (MELD) score for adult recipients and the Pediatric End-Stage Liver Disease (PELD) score for pediatric recipients. PELD score is not required for listing but may be used for the purpose of assigning priority for organ allocation. Definitions and calculators for the MELD and PELD scores can be found on the Organ Procurement and Transplant Network (OPTN) website at:
optn.transplant.hrsa.gov/resources/allocation-calculators/

- Adults with hepatocellular carcinoma (HCC) who meet Milan criteria (Mazzaferro, 1996) will be awarded MELD exception points. OPTN Dynamic Imaging criteria apply. See "Special Considerations" below.
  - Milan criteria (Mazzaferro, 1996)
    - Not a candidate for subtotal hepatic resection
    - Tumor is HCC stage II (T2 one nodule 2.0–5.0 cm, 2 or 3 nodules, all ≤ 3.0 cm)
    - No macrovascular involvement
    - No identifiable extrahepatic spread of tumor to surrounding lymph nodes, lungs, abdominal organs, or bone
  - Tumors can be downstaged with hepatic artery chemoembolization (HACE, also known as TACE) with or without radiofrequency ablation (RFA). If successfully downstaged to be within the Milan criteria, MELD exception points are not automatically assigned. All such candidates with HCC, including those with downsized tumors whose original or presenting tumor was greater than a stage T2, must be referred to the applicable Regional Review Board (RRB) for prospective review in order to receive additional priority.
- Children with the following conditions will be awarded PELD exception points:
  - Hepatoblastoma
  - Urea cycle disorders and organic acidemia
  - Combined liver/intestine transplant
- Living donor liver transplant (LDLT). See "Indications" below.
  - Results from A2ALL (Berg et al., 2011; Olthoff et al., 2015) study demonstrated significant survival advantage associated with receipt of LDLT in comparison to continued waiting for deceased donor liver transplant (DDLT) for candidates with low laboratory MELD scores.
  - Complications of cirrhosis with low MELD score should be considered for LDLT (Koffron et al., 2008).
- Patients with primary oxalosis with ESRD should be considered for combined liver/kidney transplant (Eason et al., 2008; Compagnon et al. 2014).
- Alcohol- associated liver disease has emerged as the most common indication for liver transplant, leading to a doubling of transplants in the U.S. over the past 15 years. While broader acceptance of waiving mandated periods of sobriety for this subset of patients has contributed to this increase, regional differences may be leading to inequity in transplant access (Lee et al., 2019).
- Some transplant centers may use instruments such as Maddrey's Discriminant Function (Maddrey et al., 1978), the Sustained Alcohol Use Post-LT (SALT) (Lee et al., 2019), or the Penn Alcohol Craving Scale (PACS) (Flannery et al., 1999) to assist in the identification of patients who are at low risk for continued alcohol use and thus are good candidates for liver transplant.
- Transplant in the setting of non-resectable colorectal liver metastases is emerging as a potential treatment option for select patients. Optum will continue to monitor the medical literature for outcomes data and the establishment of standardized patient selection criteria.

Indications

- Candidate for evaluation consistent with the practice guideline of the American Association for the Study of Liver Disease (AASLD) and the American Society of Transplantation (Martin et al., 2014)
- Liver transplant candidate consistent with Organ Procurement and Transplant Network (OPTN) guidelines.
    - Transplantation is indicated for patients with end-stage liver disease (ESLD) with a life expectancy < 12-24 months OR who have developed life-threatening complications or with severe liver associated debility frequently associated with sustained portal hypertension.
        - Intractable ascites usually requiring frequent paracenteses
        - Recurring variceal bleeding not well controlled with surgical banding and medical therapy
        - Recurring spontaneous bacterial peritonitis (SBP)
        - Intractable hepatic encephalopathy
        - Severe thrombocytopenia with complications
        - Intractable pruritus
        - Muscle wasting due to liver disease with other systemic illnesses excluded
        - Debilitating fatigue due to liver disease with other systemic illnesses excluded
        - Intractable hyponatremia
        - Hepatic chylothorax
- Living donor liver transplant is a valid treatment option for patients with low MELD scores, especially in cases where a deceased donor offer is not likely to occur.
- Polycystic liver disease with massive enlargement leading to physical impairment
- Hepatocellular carcinoma within Milan criteria determined by the OPTN Dynamic Imaging criteria and no CONTRAINDICATIONS
    - Not a candidate for subtotal resection
    - The HCC meets the definition of a Stage T2 lesion(s) that include any of the following:
        - One lesion greater than or equal to 2 cm and less than or equal to 5 cm in size
        - Two or 3 lesions greater than or equal to 1 cm and less than or equal to 3 cm in size
    - Written documentation has been submitted with the request that the lesion meets the definition of OPTN Class 5B, 5T or a combination of 5A lesions that meets the definition of tumor Stage T2
    - No macrovascular involvement
    - No identifiable extrahepatic spread of tumor to surrounding lymph nodes, lungs, abdominal organs, or bone
- Hepatocellular carcinoma that has been downstaged:
    - Note: Successful downstaging does not result in an automatic award of MELD exception points. The case must be referred to the Regional Review Board with a request for exception points.
    - The inclusion criteria for downstaging should be a single tumor < 8 cm or 2 to 3 tumors, each < 5 cm, with a total tumor diameter < 8 cm and no vascular invasion by imaging criteria.
    - The tumor must meet the Milan criteria after the downstaging procedure(s).
    - Successful downstaging also requires a significant decrease in the AFP level to < 500 ng/ml for those patients with an initial AFP level > 1000 ng/ml.
- Cholangiocarcinoma (Martin et al., 2014). Refer to Medical Director with protocol.
    - May be approved under certain circumstances under the appropriate protocol at a center with an approved living donor liver transplant program OR a program in a region where the RRB will award MELD exception points to patients who qualify under the requesting program's treatment protocol (Heimbach et al., 2006; Becker et al., 2008; Gores et al., 2006).

- Neuroendocrine tumors (NET). CMS has concluded: “It is unclear which patients could benefit in this rare disease, but some patients do appear to benefit from a transplant. Therefore, coverage of this treatment may be best considered only in carefully selected patients on a case-by-case basis at this time.” (Martin et al., 2014)
- Hemangioendothelioma (HAE). CMS and AASLD have concluded that generally patients with HAE have a better prognosis than do patients with HCC and may not have evidence of significant underlying liver disease. Consequently, transplantation is not common, but not necessarily contraindicated. For patients with large tumors, liver transplantation should be considered for patients with unresectable HAE (Martin et al., 2014). Refer to Medical Director.
- Hepatoblastoma: Children with hepatoblastoma may be considered for transplantation. The patient will have received multidisciplinary tumor board review and appropriate consideration of chemotherapy. PELD rules are not applied for patient selection.
  - If extrahepatic disease is not resectable or the patient is not a transplant candidate, additional chemotherapy, TACE, or radiation therapy may be indicated.
- Nonresectable hilar or perihilar cholangiocarcinoma when all of the following are met (Breuer et al., 2022; Cambridge et al., 2021): Refer to Medical Director.
  - Tumor diameter < 3 cm
  - Negative lymph nodes
  - Absence of intra- or extrahepatic metastases
- Retransplantation is usually due to primary non-function, hepatic artery thrombosis, portal vein thrombosis, rejection, chronic cholestasis without chronic rejection and recurrent disease.

Organ-specific contraindications

Please review the Universal Contraindications found at the beginning of the Guidelines. These apply to all transplants unless otherwise noted below. Additional contraindications that are specific to a particular type of transplant are noted below. When a contraindication is present, the transplant will not be approved. Refer to the Medical Director.

Unless otherwise annotated, these recommendations are consistent with the 2013 American Association for the Study of Liver Disease (AASLD) Clinical Practice Guidelines (Martin et al., 2014):

- Active untreated or untreatable non-hepatic malignancy
- Hepatocellular carcinoma that exceeds University of California, San Francisco (UCSF) criteria:
  - Single lesion not exceeding 6.5 cm; OR
  - 2–3 lesions, none exceeding 4.5 cm, WITH
  - Total tumor diameter not greater than 8 cm
- Congenital abnormalities that will preclude a liver transplant

Considerations for substance use disorder

For patients experiencing catastrophic decompensation where a period of abstinence is not realistic the transplant center must have an institutional protocol that requires, at a minimum:

- Appropriate patient and psychosocial support profile. Transplant center must have an institutional protocol to conduct psychosocial evaluation and proactively implement interventions to promote post-transplant success.
  - Presence of close supportive social network
  - Absence of severe coexisting behavioral health disorders that would negatively impact a treatment plan
  - Agreement by patient (with support of his/her social network) to post-transplant rehabilitation and monitoring, and to lifelong abstinence from addictive substances

- Evaluation by addiction specialist indicating high likelihood of success of post-transplant rehabilitation and abstinence
- Approval by a transplant selection committee that includes in addition to the regular members, a psychiatrist and/or an addiction specialist
- No special consideration for acute decompensation with illicit drug addiction and/or abuse
- Any other substance abuse needs to be addressed
- Inactive alcohol and/or substance abuse (alcohol, crystal meth, heroin, cocaine, methadone, and/or narcotics, etc.) is not a contraindication

Special considerations

Additional consultation and/or evaluation may be indicated in these situations. Refer to Medical Director if questions remain.

Unless otherwise annotated, these recommendations are consistent with the 2013 American Association for the Study of Liver Disease (AASLD) Clinical Practice Guidelines (Martin et al., 2014).

- Additional considerations may be present where liver transplantation may be appropriate in other circumstances where quality of life considerations become paramount.
    - Conditions eligible for MELD exception points:
        - Cystic fibrosis with signs of reduced pulmonary function with forced expiratory volume at one second (FEV_1) that falls below 40 percent
        - Portopulmonary hypertension
        - Hepatic artery thrombosis within 14 days of transplant
        - Hepatoblastoma (pediatric) eligible for PELD exception points
        - Urea cycle disorder or organic acidemia (pediatric) eligible for PELD exception points
        - Primary oxaluria eligible for MELD exception points
        - Hepatopulmonary syndrome eligible for MELD exception points
        - Combined liver/intestine or multivisceral transplant
        - Familial amyloidosis/familial amyloid polyneuropathy (FAP):

Patients may have no measurable abnormality of liver function at the time of the request for authorization.

Liver transplants generally are done below the age of 30 AND when the patients are clinically well.

Patients may be living donors for a “domino transplant.”

    - All other presentations not eligible for automatic MELD exception points including, but not limited to, intractable pruritus (itching), recurrent spontaneous bacterial peritonitis, bleeding, ascites, thrombocytopenia, encephalopathy, polycystic liver disease or other quality of life issues not adequately accounted for in the MELD/PELD score may be considered.
- Social and psychiatric issues can have a significant impact on the outcomes of a transplant. It is expected that a psychosocial evaluation and/or psychiatry consultation is obtained as part of the standard transplant evaluation (Crone et al., 2010). The evaluation should address the following:
    - Overall functioning
    - Understanding of underlying illness and need for proposed treatment
    - History of adherence and compliance and barriers to compliance
    - Quality of relationships
    - Presence of a supportive caregiver
    - Social history, including educational level and employment history
    - Housing and living situation, including reliable transportation to attend medical visits
    - Socioeconomic status, including sufficient funding to pay for immunosuppressive medications post-transplant

    - Current and past history of alcohol and substance use and abuse
    - Current and past psychiatric history, including baseline cognitive status and coping skills
- Primary non-function or less than one year since the initial transplant may require additional evaluation to determine causative factors.
- Patients with a history of malignancy require an oncology evaluation to determine status of disease. Recommendations for suitability and timing of a solid organ transplant following successful treatment of malignancy may be found in Appendix B. The recommendations are based on Al-Adra et al. (2021).
- Patients with human immunodeficiency virus (HIV) infection must be on a highly active antiretroviral therapy (HAART) regimen and there must be documented evidence of sustained viral load suppression.
- BMI ≥ 35 kg/m^2:
    - All programs have patient selection criteria that may need to be reviewed
    - If outside the program's patient selection criteria, refer to Medical Director.
- Pediatric patients should have a normal history and physical, or if there is any indication of abnormal cardiac function, cardiology evaluation should be obtained.
- Adult patients with known heart disease including, but not limited to, heart failure, cardiomyopathy and coronary artery disease require cardiology consultation and completion of consultant's recommendations, if any.
- Gastrointestinal (GI) clearance may be indicated in patients with a history of complicated or active GI disorders.
- Significant, uncorrectable pulmonary disease. Pulmonary consultation and completion of consultant's recommendations if any are required.

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Pancreas and kidney/pancreas

General information

- There are 3 variations of pancreas and kidney/pancreas transplants:
  - Both organs can be inserted during one procedure. This is referred to as simultaneous pancreas kidney transplantation (SPK).
  - The pancreas can be transplanted after a kidney transplant. This is referred to as pancreas after kidney transplantation (PAK).
  - The pancreas can be transplanted alone. This is called pancreas transplant alone (PTA).
- SPK, PAK or PTA may be indicated in patients with either Type 1 or Type 2 diabetes. Pancreas transplantation can provide excellent outcomes for patients with labile diabetes (Gruessner, 2011). The outcomes of combined kidney pancreas transplants in Type 2 diabetics are comparable to the outcomes in Type 1 diabetics (Light et al., 2006; Nath et al., 2005).
- SPK transplant is the definitive treatment of Type 1 diabetes combined with end-stage renal disease. Long-term graft function can lead to improvement in diabetes-related complications and, in patients younger than 50 years, can lead to improved overall survival. PAK transplant and PA transplant do not result in similar improvements in patient survival, but with appropriate patient selection, they can improve quality of life by rendering the patient insulin-free (Dhanireddy, 2012).
- A pancreas transplant may be justified on the basis that patients replace daily injections of insulin with an improved quality of life, but at the expense of a major surgical procedure and lifelong immunosuppression (White, 2009).
- The rate of patient survival is approximately 97% at one year and 92% at 3 years after SPK transplantation. Similar patient survival rates are reported for PAK and PTA recipients. Graft survival is variable, depending on the type of pancreas transplant performed. The mortality among diabetics is greatly reduced by SPK transplantation compared with the waiting list; however, it is less so for solitary pancreas transplants (Redfield et al., 2016).
- Complications include graft thrombosis, bleeding, abdominal abscess, pancreatic leak, urinary tract infection and early rejection (Ablorsu, 2008). Pancreas transplant is associated with more surgical complications and higher perioperative morbidity and mortality than kidney transplant alone (Dhanireddy, 2012). There is a high incidence of kidney graft failure in SPK recipients, following a pancreas graft loss. About 50% of the kidney graft failure occurred within 3 months after the loss of the pancreas graft (Hill, 2008).
- Autologous islet cell transplantation following total pancreatectomy for non-malignant conditions is an accepted treatment to prevent the immediate onset of insulin-dependent diabetes mellitus (Bramis, 2012). Autologous islet cell transplant is not a true transplant procedure. Rather, it involves the infusion of the patient's own islet cells into his/her liver, where they will independently produce insulin.

NOTE: For Optum nurses, autologous islet cell transplant is covered under the member's medical benefit. Refer to Job Aid 9996637: TS Auto Islet Cell Transplant Notification NF/EC Process.

  - Isolating the islets from an excised pancreas must be done by an experienced laboratory and the centers performing these infusions must have extensive experience with autologous islet cell infusions and patient management post-infusion.
  - Reinfusion of the islets does not prevent the pancreatic exocrine insufficiency that follows total pancreatectomy. This is managed in the same way as for any patient who has undergone a total pancreatectomy.
  - Post-infusion management of these patients is the same as the management of any other patient at risk for the development of diabetes.
  - Autologous islet cell transplantation is a laboratory and procedural add-on to the cost of a total pancreatectomy. It should not be considered to be an organ transplant.

- Most patients will develop diabetes eventually (Dean et al., 2008). Even though the islets lodge in the liver and function normally initially, this is not a normal environment for them. The pancreas they were taken from was not normal. Because of the underlying pancreatic disease and normal loss in processing, the number and quality of islets is not normal. The reinfused islets will eventually stop functioning. But, for the time that they are functioning, the patient is protected against the immediate development of diabetes following a total pancreatectomy. However, concurrent IAT enabled a significant proportion of patients to remain independent of insulin supplementation (Bramis, 2012).

Indications

- SPK and PAK:
  - Qualifies for kidney transplant (see kidney criteria) **AND** the member is diabetic. The outcomes of combined kidney pancreas transplants in Type 2 diabetics are comparable to the outcomes in Type 1 diabetics (Light & Barhyte, 2006).
  - The criteria for covering a pancreas transplant alone are not applicable when a kidney is also being transplanted.
- PTA:
  - Type 1 diabetes mellitus with one or both of the following:
    - Labile diabetes mellitus with documented life-threatening hypoglycemic unawareness and/or frequent hypoglycemic episodes despite optimal medical management, Clark Hypoglycemic Score ≥ 4 (see Appendix C)
    - Physical or psychological inability to safely administer exogenous insulin
  - Type 2 diabetes mellitus with one of the following:
    - Labile diabetes mellitus with documented life-threatening hypoglycemic unawareness despite optimal medical management, Clark Hypoglycemic Score ≥ 4 (see Appendix C)
    - Physical or psychological inability to safely administer exogenous insulin
  - Appropriate candidates will have all of the following characteristics (Stratta, 2009):
    - Insulin requiring diabetes for > 5 years receiving ≤ 1 unit/kg/day
    - BMI ≤ 30
    - Age < 60
    - No history of major vascular events such as bilateral limb amputations and disabling CVA
    - Not actively smoking
    - Left ventricular ejection fraction ≥ 40% with no left ventricular hypertrophy
- Retransplantation is usually due to non-function of the grafted organ(s), chronic rejection, and chronic allograft pancreatitis.

Organ-specific contraindications

Please review the Universal Contraindications found at the beginning of the Guidelines. These apply to all transplants unless otherwise noted below. Additional contraindications that are specific to a particular type of transplant are noted below. When a Contraindication is present the transplant will not be approved. Refer to Medical Director.

- Significant cardiac disease (Stratta, 2009):
  - Non-correctable coronary artery disease
  - Ejection fraction (LVEF, EF) < 40%

Considerations for substance use disorder

For patients experiencing catastrophic decompensation where a period of abstinence is not realistic the transplant center must have an institutional protocol that requires, at a minimum:

- Appropriate patient and psychosocial support profile. Transplant center must have an institutional protocol to conduct psychosocial evaluation and proactively implement interventions to promote post-transplant success.
  - Presence of close supportive social network
  - Absence of severe coexisting behavioral health disorders that would negatively impact a treatment plan
  - Agreement by patient (with support of his/her social network) to post-transplant rehabilitation and monitoring, and to lifelong abstinence from addictive substances
- Evaluation by addiction specialist indicating high likelihood of success of post-transplant rehabilitation and abstinence
- Approval by a transplant selection committee that includes in addition to the regular members, a psychiatrist and/or an addiction specialist
- No special consideration for acute decompensation with illicit drug addiction and/or abuse
- Any other substance abuse needs to be addressed
- Inactive alcohol and/or substance abuse (alcohol, crystal meth, heroin, cocaine, methadone, and/or narcotics, etc.) is not a contraindication

Special considerations

Additional consultation and/or evaluation may be indicated in these situations. Refer to Medical Director if questions remain.

- Serum C-peptide:
  - Serum C-peptide measurements are not required. Transplant candidacy is based on other considerations noted elsewhere in this document (Stratta, 2009).
- Autologous islet cell transplantation (Bramis, 2012):
  - May be indicated following total pancreatectomy for non-malignant conditions.
- Primary non-function or less than one year since the initial transplant may require additional evaluation to determine causative factors.
- Social and psychiatric issues can have a significant impact on the outcomes of a transplant. It is expected that a psychosocial evaluation and/or psychiatry consultation is obtained as part of the standard transplant evaluation (Crone et al., 2010). The evaluation should address the following:
  - Overall functioning
  - Understanding of underlying illness and need for proposed treatment
  - History of adherence and compliance and barriers to compliance
  - Quality of relationships
  - Presence of a supportive caregiver
  - Social history, including educational level and employment history
  - Housing and living situation, including reliable transportation to attend medical visits
  - Socioeconomic status, including sufficient funding to pay for immunosuppressive medications post-transplant
  - Current and past history of alcohol and substance use and abuse
  - Current and past psychiatric history, including baseline cognitive status and coping skills
- Patients with a history of malignancy require an oncology evaluation to determine status of disease. Recommendations for suitability and timing of a solid organ transplant following successful treatment of malignancy may be found in Appendix B. The recommendations are based on Al-Adra et al. (2021).

- Patients with human immunodeficiency virus (HIV) infection must be on a highly active antiretroviral therapy (HAART) regimen and there must be documented evidence of sustained viral load suppression.
- BMI ≥ 35 kg/m^2:
  - All programs have patient selection criteria that may need to be reviewed.
  - If outside the program's patient selection criteria, refer to Medical Director.
- Pediatric patients should have a normal history and physical, or if there is any indication of abnormal cardiac function, cardiology evaluation should be obtained.
- Adult patients with known heart disease including, but not limited to, heart failure, cardiomyopathy and coronary artery disease require cardiology consultation and completion of consultant's recommendations, if any.
- Gastrointestinal (GI) clearance may be indicated in patients with a history of complicated or active GI disorders.
- Patients over the age of 60:
  - Not all programs are willing to list patients over the age of 60 for pancreas transplantation. Refer to the requesting program's patient selection criteria.
  - If outside the program's patient selection criteria, refer to Medical Director.
- Significant, uncorrectable pulmonary disease. Pulmonary consultation and completion of consultant's recommendations if any is required.

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Donislecel (Lantidra)

General information

On June 28, 2023, the FDA Center for Biologics Evaluation and Research (CBER) approved Lantidra (CellTrans Inc., Chicago, IL), the first allogeneic (deceased donor) pancreatic islet cell therapy for the treatment of adults with type 1 diabetes who do not achieve target glycated hemoglobin levels due to repeated episodes of severe hypoglycemia, despite intensive diabetes management. Type 1 diabetes is a chronic metabolic disease characterized by hyperglycemia secondary to destruction of pancreatic beta cells. Absolute insulin deficiency and dependence on exogenous insulin to regulate blood glucose levels are hallmarks of the disease. Type 1 diabetes accounts for 5% to 10% of all cases of diabetes (Holt et al., 2021).

FDA approval was based on the outcomes from two safety and efficacy prospective, open-label, single-arm studies that included 30 adults with Type 1 diabetes who received between one and three infusions of Lantidra. Outcomes of the combined studies demonstrated, overall, 21/30 (70%) participants achieved more than 1 year of independence from exogenous insulin while maintaining or improving glycemic control, 11/30 (37%) participants did not require insulin for between 1 and 5 years, and 10/30 (33%) participants did not require insulin for more than 5 years. A second transplant was received by 19/30 (63%) of participants; of these, 6 (31.6%) were insulin independent at the time of transplant. Three participants (10%) did not receive a second transplant because a donor organ was not available, while four participants (36.4%) did not receive a second transplant due to intolerance of immunosuppression or withdrawing from the study within 6 months. Seven of the thirty subjects (23.3%) received a third transplant; all were insulin dependent at the time of the third transplant. Three participants did not receive a third transplant due to intolerance or non-adherence with immunosuppression (FDA briefing document, 2021).

Lantidra is a cellular suspension of allogeneic pancreatic islets (islets of Langerhans) in buffered transplant media. Each infusion lot consists of islets manufactured from the pancreas of a single deceased donor and is administered as a single infusion into the hepatic portal vein via percutaneous or transvenous access, or if these approaches are not feasible, laparoscopic, or open surgical access may be used. The primary mechanism of action is believed to be the secretion of insulin by transplanted β- cells. Long-term immunosuppression is required to prevent islet graft rejection. The immunosuppression regimen typically includes a combination of a calcineurin inhibitor and an mTOR inhibitor or appropriate alternatives (FDA, 2023).

Indications

Lantidra may be considered medically necessary in adults with Type 1 diabetes when the following criteria are met:

- Inability to achieve target HbA1c according to ADA recommendations (ElSayed et al., 2023) due to current repeated episodes of severe hypoglycemia despite intensive insulin management, particularly in the setting of hypoglycemia unawareness.
- Up to two subsequent infusions may be considered medically necessary when the following criteria are met:
  - Persistent glucose levels outside the upper limit of target (180 mg/dL) **AND/OR**
  - Failure to achieve insulin independence within one year of the most recent infusion
- Member should have completed the following evaluations prior to consideration for treatment with Lantidra:
  - Endocrinology evaluation including but not limited to:
    - Indications for insulin pump use
    - Continuous glucose monitoring
  - Evaluation for and treatment of potential diabetic complications as recommended in current nationally accepted guidelines including but not limited to:
    - Retinopathy
    - Neuropathy
    - Nephropathy

        - Gastroparesis
    - Proper psychosocial evaluation to determine compliance with diabetic care plan
    - Nutritional assessment

Lantidra is considered not medically necessary in the following:

- More than three infusions
- Members whose diabetes is well-controlled with insulin therapy

The following are contraindications to the use of Lantidra

- History of pancreas and/or kidney solid organ transplant
- History of portal vein thrombosis
- Concomitant diseases or conditions, including pregnancy, that contraindicate immunosuppression

Special considerations

Additional consultation and/or evaluation may be required in these situations:

- Members with a history of malignancy require an oncology evaluation to determine status of disease
- Members with known heart disease including, but not limited to, heart failure, cardiomyopathy and coronary artery disease require cardiology consultation and completion of consultant's recommendations, if any
- Members with a history of or known current hepatic disease require hepatology consultation and completion of consultant's recommendations, if any.

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Most recent posting of phase 3 results: Results Posted | Islet Transplantation in Type 1 Diabetic Patients Using the University of Illinois at Chicago (UIC) Protocol | ClinicalTrials.gov

Intestine including liver/intestine and multivisceral

General information

- Patients with intestinal failure syndromes should be managed in centers with robust intestinal failure/rehabilitation programs to take advantage of all opportunities to regain adequate function and to avoid total parenteral nutrition (TPN) with its complications and intestinal transplant (Beath et al., 2008; Torres et al., 2007). If no evaluation for intestinal rehabilitation has been performed, the member may be redirected to a program that has the capacity to perform these important evaluation and management services.
- Adaptation following disease or injury that leads to intestinal failure can occur over many months up to a year or more. The ability of the remaining gut to adapt to be able to support the patient with enteral nutrition alone is determined by a number of factors including the length of the remaining intestine, the segments remaining, the presence of an ileocecal valve, the presence or absence of the colon and general motility patterns. A number of medical and surgical interventions are possible to help many of these patients avoid transplant (Centers for Medicare and Medicaid; Fryer, 2007).
- Timelier referral of intestinal failure patients who have not yet developed end-stage liver disease may allow for an intestine only transplant (IOT), which is associated with better outcomes (Chungfat et al., 2007).
- The short-term survival of pediatric intestine recipients has significantly improved in the last decade and reached 90% at the end of the first year after transplant in high-volume intestinal transplant centers (Avitzur & Grant, 2010).

Indications

- Intestine:
  - Patients with irreversible intestinal failure with associated life-threatening complications (Fishbein, 2009)
  - Patients with secretory diarrhea of childhood may have high mortality/morbidity due to their underlying disease and therefore can be considered for intestine transplant evaluation in the absence of life-threatening complications (Ruemmele et al., 2004)
    - Dependent on TPN with cholestatic liver disease as defined by elevated direct bilirubin. If cholestasis is advanced, or cirrhosis is present, a combined liver/intestine transplant may be considered (Colomb et al., 2007)
    - Isolated intestinal transplants are performed in the presence of cholestasis only when the liver disease is felt to be reversible.
  - Inability to maintain fluid and electrolyte balance
  - Recurrent sepsis as a result of either line sepsis or intestinal stasis
  - Dependent on TPN with loss of or impending loss of (using last major vessel) vascular access
  - Non-reconstructible gastrointestinal (GI) tract
- Liver/small bowel/pancreas with or without addition of stomach or colon
  - Liver/intestine
    - One of the above

AND

    - Biopsy proven fibrotic changes within the liver indicating that the TPN associated liver dysfunction is irreversible

OR

- Clinical assessment of significant portal hypertension (such as hypersplenism) where biopsy may not be available or warranted or considered safe to perform

– Multivisceral
  - All of the above under Intestine

AND

- Technical considerations that make the anastomoses of one or more of the separate organs problematic when compared to an en bloc dissection and transplantation that requires fewer vascular and intestinal anastomoses

OR

- Desmoid tumors

OR

- Severe gastric or antroduodenal motility disorder (pseudo-obstruction) (Cruz et al., 2010)

OR

- Patients listed for multivisceral transplantation without TPN dependency require special case review (Kaufman et al., 2001)

- Retransplantation
  – May occur when there is a failed prior intestinal transplantation, including non-function of the grafted organ, acute rejection requiring enterectomy or chronic rejection.

Organ-specific contraindications

Please review the Universal Contraindications found at the beginning of the Guidelines. These apply to all transplants unless otherwise noted below. Additional contraindications and exceptions that are specific to a particular type of transplant are noted below. When a Contraindication is present the transplant will not be approved. Refer to the Medical Director.

- There are no organ-specific contraindications

Considerations for substance use disorder

For patients experiencing catastrophic decompensation where a period of abstinence is not realistic the transplant center must have an institutional protocol that requires, at a minimum:

- Appropriate patient and psychosocial support profile. Transplant center must have an institutional protocol to conduct psychosocial evaluation and proactively implement interventions to promote post-transplant success.
  – Presence of close supportive social network
  – Absence of severe coexisting behavioral health disorders that would negatively impact a treatment plan
  – Agreement by patient (with support of his/her social network) to post-transplant rehabilitation and monitoring, and to lifelong abstinence from addictive substances
- Evaluation by addiction specialist indicating high likelihood of success of post-transplant rehabilitation and abstinence
- Approval by a transplant selection committee that includes in addition to the regular members, a psychiatrist and/or an addiction specialist
- No special consideration for acute decompensation with illicit drug addiction and/or abuse
- Any other substance abuse needs to be addressed

- Inactive alcohol and/or substance abuse (alcohol, crystal meth, heroin, cocaine, methadone, and/or narcotics, etc.) is not a contraindication

Special considerations

Additional consultation and/or evaluation may be indicated in these situations. Refer to Medical Director if questions remain.

- Social and psychiatric issues can have a significant impact on the outcomes of a transplant. It is expected that a psychosocial evaluation and/or psychiatry consultation is obtained as part of the standard transplant evaluation (Crone et al., 2010). The evaluation should address the following:
    - Overall functioning
    - Understanding of underlying illness and need for proposed treatment
    - History of adherence and compliance and barriers to compliance
    - Quality of relationships
    - Presence of a supportive caregiver
    - Social history, including educational level and employment history
    - Housing and living situation, including reliable transportation to attend medical visits
    - Socioeconomic status, including sufficient funding to pay for immunosuppressive medications post-transplant
    - Current and past history of alcohol and substance use and abuse
    - Current and past psychiatric history, including baseline cognitive status and coping skills
- Patients with a history of malignancy require an oncology evaluation to determine status of disease. Recommendations for suitability and timing of a solid organ transplant following successful treatment of malignancy may be found in Appendix B. The recommendations are based on Al-Adra et al. (2021).
- Patients with human immunodeficiency virus (HIV) infection must be on a highly active antiretroviral therapy (HAART) regimen and there must be documented evidence of sustained viral load suppression.
- BMI ≥ 35 kg/m^2:
    - All programs have patient selection criteria that may need to be reviewed.
    - If outside the program's patient selection criteria, refer to Medical Director
- Pediatric patients should have a normal history and physical, or if there is any indication of abnormal cardiac function, cardiology evaluation should be obtained.
- Adult patients with known heart disease including, but not limited to, heart failure, cardiomyopathy and coronary artery disease require cardiology consultation and completion of consultant's recommendations, if any.
- Gastrointestinal (GI) clearance may be indicated in patients with a history of complicated or active GI disorders.
- Patients over the age of 60:
    - Not all programs are willing to list patients over the age of 60 for pancreas transplantation. Refer to the requesting program's patient selection criteria.
    - If outside the program's patient selection criteria, refer to Medical Director
- Significant, uncorrectable pulmonary disease. Pulmonary consultation and completion of consultant's recommendations if any is required.
- Subsequent recovery of hyperbilirubinemia with nutritional and medical management may allow for "delisting" or consideration of isolated intestine transplant if the liver has improved despite initial biopsy findings.

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Heart

General information

- Cardiac transplantation is an option for patients with end-stage heart disease. In 2019, new listings continued to increase, with 4,086 new candidates. Also in 2019, 3,597 heart transplants were performed, an increase of 157 (4.6%) from 2018; 509 transplants occurred in children and 3,088 in adults. Cardiomyopathy is the most common diagnosis among candidates, comprising 59.7% in 2019. The proportion of candidates with ventricular assist devices (VADs) at listing increased from 32.6% in 2018 to 37.1% in 2019. At year-end 2019, 253 candidates were listed for heart-kidney transplant, a substantial increase since 2009. The number of heart-lung candidates remained stable over this same period, with 74 candidates waiting in 2019. From 2017 to 2019, the number of patients removed from the transplant list increased, but fewer were removed due to improvement or being too ill for transplant. Compared with 2017, fewer patients died on the waiting list in 2019. At the end of 2019, 4 patients (0.1%) were listed as status 1, and 48 (1.4%) were status 2. Fewer patients were listed in the highest-urgency categories under the new allocation system implemented in 2018, with 50.5% listed as status 4 (Colvin et al., 2021).
- Combined heart-liver transplants (CHLT) have steadily increased from a total of 18 in 2016 to 73 in 2023 with United Network for Organ Sharing (UNOS) regions 3, 4, 5, 7, 9, and 11 each performing more than 30 over the same time period (OPTN, May 24, 2024) Congenital heart disease with subsequent irreversible liver dysfunction due to congestive hepatopathy has become the most common indication for CHLT (Tracy et al., 2023). In a comprehensive analysis of UNOS data on 1,084 adults who underwent heart transplant (HT) from 2009 through March 2020 [817 CHD heart-only, 74 CHD CHLT, 179 non-CHD heart-only, and 14 heart-liver-kidney], Cotter et al. (2021) found the number of CHLTs for CHD increased from a prior rate of 4/year to 21/year in 2019, representing a > 5-fold increase compared to a doubling of the CHD HT-only and non-CHD HLT groups. The analysis also noted a trend to reduced mortality in the CHD CHLT recipients associated with higher-volume centers that average one CHD CHLT annually. Additionally, in a separate retrospective analysis of the UNOS database for heart transplantation from 1987 to 2015 and stratified into patients undergoing CHLT (n = 192), heart-kidney transplantation (n=1,174), and heart-only transplantation (n=61,471), Chou et al. (2019) documented an immunoprotective effect of the simultaneously transplanted liver or kidney that is transferred to the cardiac allograft in the case of HLT and HKT.
- Ventricular Assist Devices: Please refer to the Optum Mechanical Circulatory Support Devices Guideline available internally in Knowledge Library.
- SynCardia Total Artificial Heart:
  - A total artificial heart (TAH) can maintain the life of a patient with biventricular heart failure when there is imminent risk of death with no other appropriate medical or surgical options, when the patient is waiting for a donor heart or is being evaluated for transplant, is not a candidate for LVAD or BiVAD, and there is adequate space in the chest area for the device.

Indications

Patients being considered for heart transplant may have documented one or more of the following:

- Likelihood of death from heart disease within 12–24 months without transplant
- Refractory heart failure requiring continuous inotropic support (Mehra et al., 2016)
- New York Heart Association Class III or IV or American Heart Association Stage D (Mehra et al., 2016). See Appendix D for description of heart failure categories.
- Valvular heart disease with left ventricular dysfunction (not correctable with valve replacement or repair) (Rosa et al., 2015).

- Recurrent life-threatening arrhythmias not otherwise correctable despite maximal antiarrhythmic and all appropriate conventional medical and surgical modalities (including implantable devices and multiple firings from an ICD for documented VT and VF) (Acker & Jessup, 2011)
- Intractable angina with coronary artery disease despite maximal medical therapy that is not amenable to revascularization (Yamani & Taylor, 2010)
- Primary cardiac tumors confined to the myocardium, with a low likelihood of metastasis at time of transplantation (Yamani & Taylor, 2010)
- Refractory heart failure requiring continuous inotropic (medications that support cardiac muscle contraction) support
- Severe hypertrophic or restrictive cardiomyopathy, with NYHA Class IV symptoms (Yamani & Taylor, 2010). See Appendix D for description of heart failure categories.
- Congenital heart disease (CHD) that is not amenable to surgical therapy or that has failed previous surgical correction (Patel, 2009)
- Cardiac amyloidosis, light chain (AL) or transthyretin (ATTR) type:
  - If evidence of extracardiac amyloidosis is present on biopsy, it must be deemed not likely to affect post-transplantation recovery (American College of Cardiology [ACC], 2023; Barrett et al., 2020)
  - Extracardiac involvement does not preclude cardiac transplantation but requires an extensive evaluation
  - Refer requests for transplantation in patients with cardiac amyloidosis to Medical Director
- Simultaneous heart/kidney transplant:
  - Heart transplant candidates with an established GFR < 30ml/min/1.73 m^2 or who are on dialysis may be considered for simultaneous heart kidney transplant (Kobashigawa et al., 2021)
  - If there is evidence of CKD and/or AKI not reversible despite optimizing cardiac function, the patient would be considered to have established kidney disease and may be a candidate for simultaneous heart/kidney transplant (Kobashigawa et al., 2021)
  - Candidates for simultaneous heart/kidney transplantation must undergo evaluation by both organ transplantation teams (Johnson & Nadim, 2021)
  - Refer requests for heart/kidney transplantation to Medical Director
- Combined heart liver transplantation for the following indications (Alexopoulos et al., 2022; Zhao et al., 2019):
  - Primary heart disease with secondary cardiac cirrhosis caused by chronic hepatic venous outflow obstruction including:
    - Patients with CHD that required Fontan procedure who ultimately experienced progressive hepatic fibrosis
  - Hereditary transthyretin (ATTR) amyloidosis leading to cardiomyopathy
  - Patients with primary indication for liver transplant with concurrent heart disease such as:
    - Arrhythmogenic right ventricular cardiomyopathy
    - Hypertrophic cardiomyopathy
    - Dilated nonischemic and ischemic cardiomyopathy
    - Congenital constrictive and radiation-induced cardiomyopathy
    - Sarcoidosis
- Retransplantation due to primary graft failure, rejection refractory to immunosuppressive therapy and graft coronary artery disease with severe ischemia of the heart graft. Retransplantation appears most appropriate for those patients more than 6 months following original heart transplantation, who have severe cardiac allograft vasculopathy and associated left ventricular dysfunction, or allograft dysfunction and progressive symptoms of heart failure in the absence of acute rejection (Mehra et al., 2016).

Organ-specific contraindications

Please review the Universal Contraindications found at the beginning of the Guidelines. These apply to all transplants unless otherwise noted below. Additional contraindications and exceptions specific to a particular type of transplant are noted below. When a Contraindication is present the transplant will not be approved. Refer to the Medical Director.

Unless otherwise cited, these recommendations are consistent with the 2016 International Society for Heart Lung Transplantation (ISHLT) Listing Criteria for Heart Transplantation: A 10-year update (Mehra et al., 2016):

- Significant peripheral vascular disease not correctable with surgery
- Significant uncorrectable life-limiting medical conditions such as severe end-stage organ damage including severe diabetes mellitus with end organ damage, irreversible severe pulmonary disease, with FEV_1 < 1 L or FVC < 50%, irreversible severe hepatic disease, irreversible severe renal disease, etc. (Acker & Jessup, 2011)
- Active systemic and/or uncontrolled infection associated with left ventricular assist device
- Ongoing tobacco use. It is reasonable to consider active tobacco smoking as a relative contraindication to transplantation. Active tobacco smoking during the previous 6 months is a risk factor for poor outcomes after transplant (Mehra et al., 2006; upheld by Mehra et al., 2016).

Considerations for substance use disorder

For patients experiencing catastrophic decompensation where a period of abstinence is not realistic the transplant center must have an institutional protocol that requires, at a minimum:

- Appropriate patient and psychosocial support profile. Transplant center must have an institutional protocol to conduct psychosocial evaluation and proactively implement interventions to promote post-transplant success.
  - Presence of close supportive social network
  - Absence of severe coexisting behavioral health disorders that would negatively impact a treatment plan
  - Agreement by patient (with support of his/her social network) to post-transplant rehabilitation and monitoring, and to lifelong abstinence from addictive substances
- Evaluation by addiction specialist indicating high likelihood of success of post-transplant rehabilitation and abstinence
- Approval by a transplant selection committee that includes in addition to the regular members, a psychiatrist and/or an addiction specialist
- No special consideration for acute decompensation with illicit drug addiction and/or abuse
- Any other substance abuse needs to be addressed
- Inactive alcohol and/or substance abuse (alcohol, crystal meth, heroin, cocaine, methadone, and/or narcotics, etc.) is not a contraindication

Special considerations

Additional consultation and/or evaluation may be indicated in these situations. Refer to Medical Director if questions remain.

Unless otherwise annotated, these recommendations are consistent with the 2016 International Society for Heart Lung Transplantation (ISHLT) Listing Criteria for Heart Transplantation: A 10-year update (Mehra et al., 2016) and The International Society for Heart and Lung Transplantation (ISHLT) guidelines for the care of heart transplant recipients (Velleca et al. 2022).

- Severe, irreversible pulmonary hypertension:

  - Pulmonary artery systemic pressure > 60 mm Hg, mean transpulmonary gradient > 15 mm Hg, and/or pulmonary vascular resistance (PVR) > 5 Wood units on maximal vasodilator therapy (Alba, 2010). However, the patient may qualify for combined heart/lung transplantation.
  - Elevated PVR defined as a PVR > 5 Woods units, a PVR index >6, or a transpulmonary pressure gradient 16 to 20mmHg, should be considered as relative contraindications to isolated cardiac transplantation if these parameters can't be met with optimal medication and short-term mechanical support (Optum Thoracic Solid Organ and VAD Expert Panel, 2021).
  - The current recommended practice is to perform right heart catheterization, treat with vasodilator, intraaortic balloon pump (IABP) and/or mechanical circulatory support device and follow with serial right heart catheterization. If the PA pressure and PVR do not respond to these interventions after 3 to 6 months, it is reasonable to conclude that pulmonary artery hypertension is irreversible (Mehra et al., 2016).
  - All programs have patient selection criteria that may need to be reviewed.
- Primary non-function or less than one year since the initial transplant may require additional review to determine causative factors. For Optum case managers, submit a Quality of Care referral to the Clinical Sciences Institute at: Clinical Sciences Institute - Quality of Care Referral Form - All Documents (sharepoint.com)
- Significant chronic pulmonary disease defined as FVC < 50%, non-reversible FEV1 < 50 % and DLCO (corrected) < 40 % for adults (< 50 % in children) requires pulmonary clearance.
- Diabetes with end-organ damage other than nonproliferative retinopathy or poor glycemic control ($HgbA_{1C}$ > 7.5 or 55 mmol/mol) despite optimal effort is a relative contraindication for transplant.
- Patients with a history of malignancy require an oncology evaluation to determine status of disease. Recommendations for suitability and timing of a solid organ transplant following successful treatment of malignancy may be found in Appendix B. The recommendations are based on Al-Adra et al. (2021).
- Social and psychiatric issues can have a significant impact on the outcomes of a transplant. It is expected that a psychosocial evaluation and/or psychiatry consultation is obtained as part of the standard transplant evaluation (Dew et al., 2018). The evaluation should address the following:
  - Overall functioning
  - Understanding of underlying illness and need for proposed treatment
  - History of adherence and compliance and barriers to compliance
  - Quality of relationships
  - Presence of a supportive caregiver
  - Social history, including educational level and employment history
  - Housing and living situation, including reliable transportation to attend medical visits
  - Socioeconomic status, including sufficient funding to pay for immunosuppressive medications post-transplant
  - Current and past history of alcohol and substance use and abuse
  - Current and past psychiatric history, including baseline cognitive status and coping skills
- Patients with human immunodeficiency virus (HIV) infection must be on a highly active antiretroviral therapy (HAART) regimen and there must be documented evidence of sustained viral load suppression.
- BMI > 35 kg/m^2:
  - All programs have patient selection criteria that may need to be reviewed.
  - If outside the transplant center's patient selection criteria, refer to Medical Director.
- Patients over the age of 70:

    - Not all programs are willing to list patients over the age of 70 for heart transplantation. Refer to the requesting program's patient selection criteria.
    - If outside the transplant center's patient selection criteria, refer to Medical Director.
- Clinically severe symptomatic cerebrovascular disease, including a prior cerebrovascular event, may be a relative contraindication (Mehra et al., 2016).
- Acute pulmonary embolism may be a relative contraindication (Mancini & Lietz, 2010; Alraies et al., 2014).
- Gastrointestinal (GI) clearance may be indicated in patients with a history of complicated or active GI disorders.

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Lung

General information

- The indications for lung transplantation include a diverse array of pulmonary diseases of the airways, parenchyma, and vasculature.
- According to the Consensus Document for the Selection of Lung Transplant Candidates: An Update from the International Society for Heart and Lung Transplantation (Leard et al., 2021), lung transplantation should be considered in adults with chronic end-stage lung disease who meet both of the following criteria:
  - High (>50%) risk of death from lung disease within 2 years if lung transplantation is not performed
  - High (>80%) likelihood of 5-year post-transplant survival from a general medical perspective provided that there is adequate graft function
- In early 2023, the OPTN implemented policy change that better aligns lung allocation policy regulatory requirements, community and ethical goals identified by OPTN, and medical advancements, while considering each candidate holistically. It moves lung allocation into a continuous distribution framework, removes rigid boundaries in lung allocation, and introduces the composite allocation score for lung candidates (OPTN, March 2023).
- The lung composite allocation score (CAS) is the combined total of the candidate's lung medical urgency score, lung post-transplant outcomes score, lung biological disadvantages score, and lung placement efficiency score. The lung CAS is awarded on a scale from 0 to 100. The lung CAS calculator may be found at: Lung Composite Allocation Score (CAS) Calculator - OPTN (hrsa.gov)
- Emerging data suggest an association between frailty and greater morbidity and mortality pre- and post-transplantation. Frailty measurements pretransplant offer the potential for improving risk stratification and refining candidate selection (Kobashigawa et al., 2019).
- The choice of single or double lung transplantation is a clinical decision that is left to the treating physicians.
- Simultaneous referral to palliative care at the time of transplant evaluation may be appropriate to provide decision support and treatment selection that is consistent with goals of care throughout the evaluation, listing, surgery, and post-transplant periods (Leard et al., 2021).

Indications

Unless otherwise cited, the following disease-specific criteria are consistent with the Consensus Document for the Selection of Lung Transplant Candidates: An Update from the International Society for Heart and Lung Transplantation (Leard et al., 2021).

- Chronic Obstructive Pulmonary Disease (COPD)
  - Clinical deterioration despite maximal treatment including medication, pulmonary rehabilitation, oxygen therapy, and as appropriate, nocturnal non-invasive positive pressure ventilation
  - BODE score 7–10 *and any of the following:*
    - FEV_1 < 20% predicted
    - Moderate to severe pulmonary hypertension
    - History of severe exacerbations
    - Chronic hypercapnia
- Cystic fibrosis (CF):
  - FEV_1 < 30% predicted in adults (or < 40% predicted in children)

- FEV_1 < 40% predicted in adults (or < 50% predicted in children) *and any of the following:*
  - Six-minute walk distance < 400 meters
  - P_aCO_2 > 50 mmHg
  - Hypoxemia at rest or with exacerbation
  - Pulmonary hypertension (PA systolic pressure > 50 mmHg on echocardiogram or evidence of right ventricular dysfunction)
  - Worsening nutritional status particularly with BMI < 18 kg/m^2 despite nutritional intervention
  - Frequent hospitalization, particularly if > 28 days hospitalized in the preceding year
  - Any exacerbation requiring mechanical ventilation
  - Chronic respiratory failure with hypoxemia or hypercapnia
  - Recurrent massive hemoptysis despite bronchial artery embolization
  - World Health Organization functional class IV
- Non-CF bronchiectasis
  - Similar criteria as with CF (identified above) is reasonable, recognizing that prognosis is highly variable with many patients experiencing a more stable course
- Interstitial lung disease (ILD), including idiopathic pulmonary fibrosis (IPF)
  - Any form of pulmonary fibrosis with one of the following in the past 6 months despite optimal treatment:
    - Absolute decline in FVC > 10%
    - Absolute decline in DLCO > 10%
    - Absolute decline in FVC > 5% with radiographic progression
  - Desaturation to < 88% in 6-minute walk test or > 50 m decline in 6-minute walk test distance in the past 6 months
  - Pulmonary hypertension on right heart catheterization or 2-dimensional echocardiography (in the absence of diastolic dysfunction)
  - Hospitalization due to respiratory decline, pneumothorax, or acute exacerbation
- Pulmonary arterial hypertension (PAH):
  - ESC/ERS (European Society of Cardiology/European Respiratory Society) high risk or REVEAL (Registry to Evaluate Early and Long-term Pulmonary Arterial Disease Management) risk score > 10 on appropriate PAH therapy, including IV or SC prostacyclin analogues
  - Progressive hypoxemia
  - Progressive, but not end-stage, liver, or kidney dysfunction due to PAH
  - Life-threatening hemoptysis
- Acute respiratory distress syndrome (ARDS), including COVID-19-associated ARDS
  - Persistent requirement for mechanical ventilatory support and/or extracorporeal life support without expectation of clinical recovery and evidence of irreversible lung destruction
  - In patients diagnosed with COVID-19-associated ARDS the following must be met: (Bharat et al., 2021)
    - At least 4 weeks have elapsed since the onset of severe acute respiratory syndrome, unless potentially lethal pulmonary complications exist that cannot be managed medically or through the use of ECMO
    - Lung recovery is deemed unlikely by at least 2 physicians from 2 different specialties (surgery, critical care, or pulmonary medicine) despite optimized medical care
    - Two negative PCR tests of bronchoalveolar lavage fluid are obtained, 24 hours apart
    - If separated from the ventilator with no tracheostomy, 2 negative PCR tests of nasopharyngeal swabs are obtained, 24 hours apart
    - When available, viral cultures are negative, confirming the absence of replication-competent virus; bronchoalveolar lavage should be used when possible

  - There may be pathological reasons other than COVID-related ARDS, such as pulmonary fibrosis, for which lung transplant may be indicated. Refer such requests to the Medical Director.

- Multi-organ transplantation:
  - Member should meet the criteria for lung transplant listing and have significant dysfunction of one or more additional organs or meet the listing criteria for a non-pulmonary organ transplant and have significant pulmonary dysfunction.
  - Refer requests for multi-organ transplantation to the Medical Director.

Organ-specific contraindications

Please review the Universal Contraindications found at the beginning of the Guidelines. These apply to all transplants unless otherwise noted below. Additional contraindications that are specific to a particular type of transplant are noted below. When a contraindication is present the transplant will not be approved. Refer to the Medical Director.

Unless otherwise annotated, these recommendations are consistent with the International Society for Heart and Lung Transplantation (ISHLT) Consensus Document for the Selection of Lung Transplant Candidates (Leard et al., 2021)

- Significant chest wall/spinal deformity (Moreno, 2008)
- Active substance use or dependence that is deemed by the treating team to negatively impact the patient and/or the transplanted organ, including current tobacco use, vaping, marijuana smoking, or IV drug use
- Glomerular filtration rate < 40 mL/min/1.73m^2 unless being considered for multi-organ transplant
- Acute coronary syndrome or myocardial infarction within 30 days (excluding demand ischemia)
- Stroke within 30 days
- Liver cirrhosis with portal hypertension or synthetic dysfunction unless being considered for multi-organ transplant
- Acute liver failure
- Acute renal failure with rising creatinine or on dialysis and low likelihood of recovery

Considerations for substance use disorder

For patients experiencing catastrophic decompensation where a period of abstinence is not realistic the transplant center must have an institutional protocol that requires, at a minimum:

- Appropriate patient and psychosocial support profile. Transplant center must have an institutional protocol to conduct psychosocial evaluation and proactively implement interventions to promote post-transplant success.
  - Presence of close supportive social network
  - Absence of severe coexisting behavioral health disorders that would negatively impact a treatment plan
  - Agreement by patient (with support of his/her social network) to post-transplant rehabilitation and monitoring, and to lifelong abstinence from addictive substances
- Evaluation by addiction specialist indicating high likelihood of success of post-transplant rehabilitation and abstinence
- Approval by a transplant selection committee that includes in addition to the regular members, a psychiatrist and/or an addiction specialist
- No special consideration for acute decompensation with illicit drug addiction and/or abuse
- Any other substance abuse needs to be addressed
- Inactive alcohol and/or substance abuse (alcohol, crystal meth, heroin, cocaine, methadone, and/or narcotics, etc.) is not a contraindication

Special considerations

Additional consultation and/or evaluation may be indicated in these situations.

Unless otherwise cited, the following disease-specific criteria are consistent with the Consensus Document for the Selection of Lung Transplant Candidates: An Update from the International Society for Heart and Lung Transplantation (Leard et al., 2021).

- Primary non-function of less than one year since the initial transplant may require additional review to determine causative factors.
- Patients with a history of malignancy require an oncology evaluation to determine status of disease. Recommendations for suitability and timing of a solid organ transplant following successful treatment of malignancy may be found in Appendix B. The recommendations are based on Al-Adra et al. (2021).
- Social and psychiatric issues can have a significant impact on the outcomes of a transplant. It is expected that a psychosocial evaluation and/or psychiatry consultation is obtained as part of the standard transplant evaluation (Dew et al., 2018). The evaluation should address the following:
    - Overall functioning
    - Understanding of underlying illness and need for proposed treatment
    - History of adherence and compliance and barriers to compliance
    - Quality of relationships
    - Presence of a supportive caregiver
    - Social history, including educational level and employment history
    - Housing and living situation, including reliable transportation to attend medical visits
    - Socioeconomic status, including sufficient funding to pay for immunosuppressive medications post-transplant
    - Current and past history of alcohol and substance use and abuse
    - Current and past psychiatric history, including baseline cognitive status and coping skills
- Mechanical ventilation and ECMO.
- Patients with human immunodeficiency virus (HIV) infection must be on a highly active antiretroviral therapy (HAART) regimen and there must be documented evidence of sustained viral load suppression.
- BMI > 35 kg/m^2:
    - All programs have patient selection criteria that may need to be reviewed.
    - If outside the program's patient selection criteria, refer to Medical Director.
- BMI < 16 kg/m^2:
    - All programs have patient selection criteria that may need to be reviewed.
- Gastrointestinal (GI) clearance may be indicated in patients with a history of complicated or active GI disorders.
- Patients over the age of 70 years:
    - Refer to the requesting program's patient selection criteria.
- The presence of other medical comorbidities such as diabetes mellitus, osteoporosis, gastroesophageal reflux, and coronary artery disease must be assessed individually based on severity of disease, presence of end-organ damage and ease of control with standard therapies (Lee, 2010).
    - Refer to the requesting program's patient selection criteria.

References

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Heart/Lung

General information

In 2023 54 heart/lung transplants were completed, 1 of which was a child, according to OPTN (2023).

Indications

- Patients with end-stage pulmonary vascular disease with end-stage non-reversible cardiac disease secondary to one of the following:
    - Primary pulmonary hypertension
    - Eisenmenger syndrome with a cardiac defect not correctable by surgical repair
    - Patients who are appropriate for single or double lung transplantation and who have severe cardiac disease not otherwise treatable

Organ-specific contraindications

Please review the universal contraindications found at the beginning of the Guidelines. These apply to all transplants unless otherwise noted below. Additional contraindications specific to a particular type of transplant are noted below. When a contraindication is present the transplant will not be approved. Refer to the Medical Director.

- Refer to the organ-specific contraindications in both the heart and lung transplantation sections of the Guidelines.

Considerations for substance use disorder

For patients experiencing catastrophic decompensation where a period of abstinence is not realistic the transplant center must have an institutional protocol that requires, at a minimum:

- Appropriate patient and psychosocial support profile. Transplant center must have an institutional protocol to conduct psychosocial evaluation and proactively implement interventions to promote post-transplant success.
    - Presence of close supportive social network
    - Absence of severe coexisting behavioral health disorders that would negatively impact a treatment plan
    - Agreement by patient (with support of his/her social network) to post-transplant rehabilitation and monitoring, and to lifelong abstinence from addictive substances
- Evaluation by addiction specialist indicating high likelihood of success of post-transplant rehabilitation and abstinence
- Approval by a transplant selection committee that includes in addition to the regular members, a psychiatrist and/or an addiction specialist
- No special consideration for acute decompensation with illicit drug addiction and/or abuse
- Any other substance abuse needs to be addressed
- Inactive alcohol and/or substance abuse (alcohol, crystal meth, heroin, cocaine, methadone, and/or narcotics, etc.) is not a contraindication

Special considerations

- Candidates for simultaneous heart/lung transplantation should undergo evaluation by both organ transplant teams.
- Recommendations for suitability and timing of a solid organ transplant following successful treatment of malignancy may be found in Appendix B. The recommendations are based on Al-Adra et al. (2021).

Reference

OPTN (2023). National data - OPTN (hrsa.gov)

Appendices

Appendix A
National Kidney Foundation Definition of Chronic Kidney Disease (CKD)

- Kidney damage for ≥ 3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifest by either:
    - Pathological abnormalities; or
    - Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests
- GFR < 60 ml/min/1.73 m^2 for ≥ 3 months, with or without kidney damage

Reference

What is the Criteria for CKD | National Kidney Foundation

Appendix B
Pretransplant solid organ malignancy and organ transplant candidacy: Recommendations for time interval to transplant

The recommendations below are adapted from the consensus expert opinion statement of the American Society of Transplantation published in 2021.

Breast cancer		
Risk/stage	**Time interval to transplant**	**Additional considerations**
Low risk DCIS Stage I	No wait time necessary after completion of all standard treatments.	Endocrine therapy does not need to be completed prior to transplant.
Intermediate risk Stage II	1–2 years, no evidence of disease after completion of all standard treatments.	Mammogram prior to transplant recommended.
High risk stage III	3–5 years, no evidence of disease after completion of all standard treatments.	
Prohibitive risk Stage V	Not a solid organ transplant candidate.	
Colon cancer		
Risk/stage	**Time interval to transplant**	**Additional considerations**
Low risk Stage I (T1 or T2, N0, M0)	1 year	Low-risk features: • MSI without BRAF mutations
Low intermediate risk Stage II (T3, N0, M0)	2 years, consider longer if high-risk features present.	High-risk features: • Lymphovascular invasion (LVI) or perineural invasion (PVI) • Mucinous, Signet or poorly differentiated histology • Bowel obstruction • Tumor perforation • < 12 lymph nodes examined Consider chemotherapy prior to transplant for high-risk stage II disease. Patients with stage III disease should complete chemotherapy.
High intermediate risk Stage II (T4, N0, M0) Stage III (Any T, N+, M0)	3 years, 5 years if high-risk features present.	
High risk Stage IV (Any T, Any N, M+)	5 years, no evidence of disease.	Transplant not recommended prior to 5 years.
Rectal cancer		
Risk/stage	**Time interval to transplant**	**Additional considerations**
Low risk Stage I (T1 or T2, N0, M0) Full oncologic resection	1 year, consider 2 years of high-risk features present.	Low-risk features: • MSI without BRAF mutations • Upper 1/3 rectum or rectosigmoid High-risk features: • LVI or PNI • Mucinous, Signet or poorly differentiated histology

		• Bowel obstruction • Tumor perforation • > 12 lymph nodes examined • Lower 1/3 of rectum • Incomplete mesorectal excision
Low intermediate risk Stage I (T1, N0, M0) Local excision	2 years	
High intermediate risk Stage II (T3 or T4, N0, M0) Stage III (Any T, N+, M0)	3 years, 5 years if high-risk features present.	Patients with stage II and III disease should complete trimodality treatment (chemoradiotherapy, surgery and chemotherapy) unless elimination of one of these is deemed appropriate after multidisciplinary discussion.
High risk Stage IV (Any T, Any N, M+)	5 years, no evidence of disease.	Transplant not recommended prior to 5 years.
Prostate cancer		
Risk/stage	**Time interval to transplant**	**Additional considerations**
Very low risk PSA < 10ng/ml 3 or fewer cores of Gleason 6 (grade group 1): no greater than 50% of individual core (T1c-T2a)	None	Surveillance strongly recommended.
Low risk PSA < 10ng/ml Gleason 6 (not meeting very low risk criteria) (T1c-T2a)	None	Surveillance strongly recommended.
Low-volume intermediate risk One of the following criteria: • PSA > 10ng/ml • Gleason 7 (grade group 2 or 3) • T2b	If surveillance, no wait time. If treatment initiated, and nomogram predicts cancer-specific death over the next 15 years < 10%, no wait time.	
High-volume intermediate risk, high risk or very high risk PSA> 20ng/ml or high-volume Gleason 7 or Gleason 8-10, T3	If treatment initiated, and nomogram predicts cancer-specific death over the next 15 years < 10%, no wait time.	
Metastatic castration-sensitive	If stable disease for 2 years with prolonged estimated life expectancy, may consider transplant.	
Metastatic castration-resistant	Not a solid organ transplant candidate.	
Renal cell carcinoma		
Stage	**Time interval to transplant**	**Additional considerations**
T1a (≤ 4cm), N0, M0	No wait time.	
T1b (> 4cm ≤ 7cm), N0, M	Fuhrman grade (FG) 1–2: no wait time. FG 3–4: 1–2 years.	
T2 (7–10cm), N0, M0	2 years	
T3, N0, M0	Minimum of 2 years, then reassess.	
T4, N0,M0	Minimum of 2 years, then reassess.	

Any T, node positive, metastatic disease	Not a candidate (if solitary metastasis +resected, tumor board discussion on candidacy.	
Any T with sarcomatoid and/or rhabdoid histologic features	Not a solid organ transplant candidate.	
Collecting duct or medullary RCC	Not a solid organ transplant candidate.	
Bladder cancer		
Bladder cancer history	**Time interval to transplant**	**Additional considerations**
Non-muscle invasive bladder cancer (NMIBC) low risk Solitary tumor ≤ 3cm, low grade, Ta, absence of carcinoma in situ (CIS)	6 months	
Intermediate risk Solitary tumor > 3cm, recurrence within 12 months with low-grade Ta tumor, multifocal low-grade Ta tumor, low-grade T1 tumor, or high-grade tumor < 3cm	6 months	
High risk Any CIS, high-grade Ta tumor > 3cm, high-grade T1 tumor, multifocal high-grade Ta tumor, any recurrent high-grade Ta tumor, variant histology, lymphovascular invasion, high-grade prostatic urethral involvement, recurrence after Bacillus Calmette-Guerin (BCG) intravesical therapy	2 years	
Muscle invasive bladder cancer (MIBC), post-radical cystectomy	2 years	
MIBC, post-chemoradiation	Not a solid organ transplant candidate.	
Gynecological cancer		
5-year risk recurrence	**Type/stage**	**Time interval to transplant**
Low risk < 5% risk of recurrence	Stage IA/IB, grade 1–2 endometrial cancer. Stage IA/IB/IC grade 1–2 epithelial ovarian cancer. Stage IA1, IA2 squamous/adenocarcinoma of cervix.	No waiting period after completion of primary treatment.
Intermediate risk 5%–15% risk of recurrence	Stage I/II endometrial cancer + risk factors (older age, lymph-vascular space invasion, grade 2 or 3 endometroid, deeply invasive tumor).	2–3 years after completion of treatment.
High risk > 30% risk of recurrence	Serous, clear cell, or carcinosarcoma of uterus (all stages). Stage III grade 1–3 endometrioid cancer of uterus. Stage II/III epithelial ovarian cancer.	5 years after completion of treatment.

	Stage II/III squamous cell/adenocarcinoma cervical cancer.	
Very high risk > 80% chance of recurrence	Stage IV endometrial cancer (all grades). Recurrent or metastatic endometrial cancer. Stage IV epithelial ovarian cancer (any grade). Stage IV squamous cell/adenocarcinoma of cervix. Metastatic or recurrent cervical cancer.	Not a solid organ transplant candidate.
Lung cancer		
Stage, tumor, and node	**Time interval to transplant**	**Workup pretransplant**
I, T1a, N0	≥ 3 years	PET-CT; consider biopsy post-stereotactic body radiation therapy (SBRT).
I, T1b, N0	≥ 3 years	PET-CT; consider biopsy post-SBRT.
I, T1c, N0	3-5 years	PET-CT; consider biopsy post-SBRT.
IB, T2a, N0	5 years	PET-CT
IIA, T2b, N0	5 years	PET-CT
IIB, T3, N0	5 years	PET-CT
IIIA	5 years	PET-CT
IIIB	Not a solid organ transplant candidate.	N/A
IIIC	Not a solid organ transplant candidate.	N/A
IVA	Not a solid organ transplant candidate.	N/A
IVB	Not a solid organ transplant candidate.	N/A

Reference

Al-Adra DP, Hammel L, Roberts J, et al. Pretransplant solid organ malignancy and organ transplant candidacy: A consensus expert opinion statement. Am J Transplant. 2021 Feb;21(2):460-474. doi: 10.1111/ajt.16318. Epub 2020 Oct 23. PMID: 32969590; PMCID: PM

Appendix C

Clarke Hypoglycemic Score

Check the category that best describes you: (check only one):

- ☐ I always have symptoms when my blood sugar is low (A)
- ☐ I sometimes have symptoms when my blood sugar is low (R)
- ☐ I no longer have symptoms when my blood sugar is low (R)

Have you lost some of the symptoms you used to have when your blood sugar was low?

- ☐ Yes (R)
- ☐ No (A)

In the past 6 months, how often have you had moderate hypoglycemia episodes? (Episodes where you might feel confused, disoriented, or lethargic and were unable to treat yourself):

- ☐ Never (A)
- ☐ Once or twice (R)
- ☐ Every other month (R)
- ☐ Once a month (R)
- ☐ More than once a month (R)

In the past year, how often have you had severe hypoglycemic episodes? (Episodes where you were unconscious or had seizure and needed glucagon or intravenous glucose):

- ☐ Never (A)
- ☐ 1 time (R)
- ☐ 2 times (R)
- ☐ 3 times (R)
- ☐ 5 times (R)
- ☐ 6 times (R)
- ☐ 7 times (R)
- ☐ 8 times (R)
- ☐ 9 times (R)
- ☐ 10 times (R)
- ☐ 11 times (R)
- ☐ 12 times (U)

How often in the last month have you had readings < 70 mg/dl with symptoms?

- ☐ Never
- ☐ 1 to 3 times
- ☐ 1 time/week
- ☐ 2 to 3 times/week
- ☐ 4 to 5 times/week
- ☐ Almost daily

How often in the last month have you had readings < 70 mg/dl without any symptoms?

- ☐ Never
- ☐ 1 to 3 times
- ☐ 1 time/week
- ☐ 2 to 3 times/week
- ☐ 4 to 5 times/week
- ☐ Almost daily

(R = answer to 5 < answer to 6, A = answer to 6 >answer to 5)

How low does your blood sugar need to go before you feel symptoms?

- ☐ 60–69 mg/dl (A)
- ☐ 50–59 mg/dl (A)
- ☐ 40–49 mg/dl (R)
- ☐ < 40 mg/dl (R)

To what extent can you tell by your symptoms that your blood sugar is low?

- ☐ Never (R)
- ☐ Rarely (R)
- ☐ Sometimes (R)
- ☐ Often (A)
- ☐ Always (A)

Hypoglycemic unawareness (Clarke score): R ≥ 4

Reference

Geddes J, Wright RJ, Zammitt NN, Deary IJ, Frier BM. An evaluation of methods of assessing impaired awareness of hypoglycemia in Type I diabetes. *Diabetes Care*. 2007;30:1868-1870.

Appendix D

New York Heart Association (NYHA) Functional Classification

Class	Patient symptoms
Class I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation (feeling heart beats), dyspnea (shortness of breath) or anginal (chest) pain.
Class II	(Mild) — Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, dyspnea or anginal pain.
Class III	(Moderate) — Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes fatigue, palpitation, dyspnea or anginal pain.
Class IV	(Severe) — Unable to carry out any physical activity without discomfort. Symptoms of cardiac insufficiency or the anginal syndrome may be present at rest. If any physical activity is undertaken, discomfort is increased.

Class	Objective assessment
A	No objective evidence of cardiovascular disease. No symptoms and no limitation in ordinary physical activity.
B	Objective evidence of minimal cardiovascular disease. Mild symptoms and slight limitation during ordinary activity. Comfortable at rest.
C	Objective evidence of moderately severe cardiovascular disease. Marked limitation in activity due to symptoms, even during less-than-ordinary activity. Comfortable only at rest.
D	Objective evidence of severe cardiovascular disease. Severe limitations. Experiences symptoms even while at rest.

Reference

Classes of Heart Failure | American Heart Association

Appendix E

American College of Cardiology/American Heart Association Stages of Heart Failure

Stage	Definition
Stage A	Patients at risk for heart failure who have not yet developed structural heart changes (i.e., those with diabetes, those with coronary disease without prior infarct)
Stage B	Patients with structural heart disease (i.e., reduced ejection fraction, left ventricular hypertrophy, chamber enlargement)
Stage C	Patients who have developed clinical heart failure
Stage D	Patients with refractory heart failure requiring advanced intervention (i.e., biventricular pacemakers, left ventricular assist device, transplantation)

Reference

ACC/AHA Heart Failure Classification | Learn the Heart (healio.com)

Review and approval history

Version	Date of annual review
1.0	07/19/2012: New.
2.0	10/10/2013: Annual review.
3.0	08/07/2014: Annual review.
4.0	08/25/2015: Annual review.
5.0	08/16/2016: Annual review.
6.0	09/07/2017: Annual review.
7.0	08/18/2018: Annual review of abdominal organ transplant content
8.0	12/05/2018: Annual review of thoracic organ transplant content
9.0	8/7/19: Annual review of abdominal solid organ content. Version effective date: 12/1/2019.
10.0	1/15/20: Annual review of thoracic solid organ content. Version effective date: 4/1/2020.
11.0	7/29/20: Annual review of abdominal solid organ content. Version effective date: 10/1/20.
12.0	2/10/21: Annual review of thoracic solid organ content. Version effective date: 4/1/21.
13.0	7/14/21: Annual review of abdominal solid organ content. Version effective date: 9/10/21.
14.0	2/23/22: Annual review of thoracic solid organ. Lung transplant indications revised for clarity. SARS-CoV2 Vaccination Statement added. Version effective date: 5/9/22.
14.0	9/27/22: Annual review of abdominal solid organ content. Added hilar and perihilar cholangiocarcinoma to liver transplant indications. Version effective date: 11/3/22.
15.0	3/1/23**:** Annual review of thoracic solid organ content. Heart liver transplant and cardiac amyloidosis indications added.
15.0	9/26/23: Annual review of the abdominal solid organ content. Medical necessity criteria added for Donislecel (Lantidra).
15.0	11/17/23: Approved by Pharmacy &Therapeutics (P&T) Committee
15.0	12/7/23: Approved by the Medical Technology Advisory Committee (MTAC)
15.0	12/13/23: Approved by the Medicare Advantage Policy and Technology Assessment Committee (MAP TAC)
16.0	8/9/24: Annual review of thoracic solid organ content. Approved by Optum Clinical Advisory Committee.
16.0	9/5/24: Approved by the Medical Technology Advisory Committee (MTAC)