Kidney Transplant

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Origination: 8/2001  Next Review: 8/2015

Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for a kidney transplant when it is determined to be medically necessary because the criteria shown below are met.

When Policy Topic is covered
Kidney transplants with either a living or cadaver donor are considered medically necessary for carefully selected candidates with end-stage renal disease.

Etiologies of end-stage renal disease include, but are not limited to any of the following conditions associated with end-stage renal disease:

- Obstructive uropathy
- Systemic Lupus Erythematosus
- Polyarteritis
- Wegener’s granulomatosis
- Cortical necrosis
- Henoch-Schonlein purpura
- Hemolytic uremic syndrome
- Acute tubular necrosis
- Hypertensive nephrosclerosis
- Renal artery or vein occlusion
- Chronic pyelonephritis
- IGA nephropathy
- Anti-glomerular base-membrane disease
- Focal glomerulosclerosis
- Analgesic nephropathy
- Heavy metal poisoning
- Glomerulonephritis
- Polycystic kidney disease
- Medullary cystic disease
- Nephritis
- Nephrocalcinosis
- Gout nephritis
- Amyloid disease
- Fabry’s disease
- Cystinosis
- Oxalosis
- Diabetes mellitus
- Horseshoe kidney
- Renal aplasia or hypoplasia
- Wilm’s tumor
- Renal-cell carcinoma
- Myeloma in remission
- Tuberous sclerosis
- Trauma requiring nephrectomy
- Goodpasture’s (Anti-glomerular base-membrane disease)

Kidney retransplant after a failed primary kidney transplant may be considered medically necessary.

**When Policy Topic is not covered**
Kidney transplant is considered investigational in all other situations.

**Considerations**
Kidney transplants should be considered for coverage under the Transplant Benefit:

Potential contraindications to solid organ transplant (subject to the judgment of the transplant center):
1. Known current malignancy, including metastatic cancer
2. Recent malignancy with high risk of recurrence
3. History of cancer with a moderate risk of recurrence
4. Systemic disease that could be exacerbated by immunosuppression
5. Untreated systemic infection making immunosuppression unsafe, including chronic infection
6. Other irreversible end-stage disease not attributed to kidney disease
7. Psychosocial conditions or chemical dependency affecting ability to adhere to therapy

HIV-positive patients who meet the following criteria, as stated in the 2001 guidelines of the American Society of Transplantation, could be considered candidates for kidney transplantation:
- CD4 count >200 cells per cubic millimeter for >6 months
- HIV-1 RNA undetectable
- On stable anti-retroviral therapy >3 months
- No other complications from AIDS (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidiosis mycosis, resistant fungal infections, Kaposi’s sarcoma, or other neoplasm), and
- Meeting all other criteria for transplantation.

Kidney Specific
Indications for renal transplant include a creatinine level of greater than 8 mg/dL, or greater than 6 mg/dL in symptomatic diabetic patients. However, consideration for listing for renal transplant may start well before the creatinine level reaches this point, based on the anticipated time that a patient may spend on the waiting list.

**Transplant Benefit**
The date on which the Transplant Benefit starts accumulating is determined by the transplant coordinator. The Transplant Benefit ends when the Transplant Lifetime Maximum benefit (if applicable) has been exhausted.

Benefits include:
- hospitalization of the recipient for medically recognized transplants from a donor to a transplant recipient;
- evaluation tests requiring hospitalization to determine the suitability of both potential (member's benefits must be verified with regard to the potential donor who does not turn out to be the actual donor) and actual donors, when such tests cannot be safely and effectively performed on an outpatient basis (Note: The member's benefits must be verified with regard to the potential donor who does not turn out to be the actual donor.);
- hospital room, board and general nursing in semi-private rooms;
- special care units, such as coronary and intensive care;
- hospital ancillary services;
- physicians’ services for surgery, technical assistance, administration of anesthetics, and medical care;
- acquisition, preparation, transportation, and storage of organ / tissue / cells;
- diagnostic services;
- drugs which require a prescription by federal law;
- medical and surgical care of the donor (related to the procurement of the organ / tissue / cells) if coverage is not available to the donor from any other source. (Covered services provided to a donor will be applied against the recipient's transplant maximum benefit, if applicable)

If the donor and recipient are both listed on the same (family) policy, BCBSKC charges only one deductible and one coinsurance, if applicable.

In addition to the specific organ criteria, transplant candidates must also meet the following general criteria, including, but not limited to:
- Since compliance is a major factor in transplant graft survival, the patient (or legal guardian) must have the ability to accept and understand the transplant procedure and to maintain compliance with long-term medical management and immunosuppression.
- If applicable, patients with a history of malignancy must have passed the recommended length of time to be considered cured for that specific cancer. A complete metastatic evaluation must be performed before a patient will be considered an acceptable transplant candidate.
- Patients with a history of alcohol or substance abuse must have a six month history of abstinence as evidenced by negative urine or serum drug screens taken randomly.
- The patient must have adequate cardiopulmonary status.
- The patient must be free from active infection.

A covered person is eligible for retransplantation as deemed medically necessary and appropriate by BCBSKC. Review of a retransplantation request will include review of the covered person's compliance with relevant transplant selection criteria including, but not limited to, adherence to medication regimens, follow-up examinations and abstinence from the use of alcohol and drugs.

Individual member contracts should be reviewed for coverage related to donors and recipients, out of network treatment, drugs and other possible limitations or exclusions.

Coverage will not be provided for:
- Transplant services when the cost is covered by government, foundation or charitable grants
- The purchase price of organs which are sold rather than donated to the recipient.
- An artificial organ

Clinical trials for conditions other than those allowed in this policy may be available in the research setting. However, these trials are considered investigational and/or experimental and therefore contract exclusions.

*Note: There are some state mandates in place that require insurance carriers to cover certain clinical trials under very specific guidelines. Please contact your BCBSKC representative for more information.*

**Description of Procedure or Service**
A kidney transplant involves the surgical removal of a kidney from a cadaver, living-related, or living-unrelated donor and transplantation into the recipient.

**Background**
Based on data from the Organ Procurement and Transplantation Network, in 2013 about 40% of kidney transplants in the U.S. (5734 of 13,280) were performed using organs from living donors. (1) As of April 2014, the 5-year survival rate for kidney transplants performed between 1997 and 2000 was 66.6% for organs from deceased donors and 79.8% for organs from living donors.
Combined kidney pancreas transplant and management of acute rejection of kidney transplant using either intravenous immunoglobulin or plasmapheresis are discussed in separate policies.

**Rationale**

This policy was originally created in 1995 and was updated regularly with searches of the MEDLINE database. The policy was updated regularly with literature searches. The most recent literature review was conducted through May 14, 2014.

**Organ donation**

Kidney transplant is an accepted treatment of end stage renal disease (ESRD) that results from a variety of etiologies, most commonly diabetic nephropathy. An insufficient supply of donor organs continues to be a challenge. A 2012 review article by Schold and Segev focused on strategies to increase the pool of organs available for kidney transplantation from deceased donors. (2) Interventions discussed included an “opt-out” policy in which persons are presumed to give consent to organ donation unless they specify nonconsent, expanded use of donors such as commercial sex workers who are considered to be at increased risk of disease transmission by using rigorous screening and expanded use of donors with documented infections in selected situations eg, transplantation of organs from HIV-positive donors to HIV-positive recipients.

**Living donors**

Several articles have reported on long-term outcomes in live kidney donors. The most appropriate control group to evaluate whether donors have increased risks of morbidity and mortality are persons who meet the criteria for kidney donation but who did not undergo the procedure. Studies of this type have had mixed findings. For example, Segev et al did not find that donors had an increased mortality risk. (3) The authors analyzed data from a national registry of 80,347 live donors in the U.S who donated organs between April 1, 1994 and March 31, 2009 and compared them with data from 9364 participants of the National Health and Nutrition Examination Survey (NHANES) (excluding those with contraindications to kidney donation). There were 25 deaths within 90 days of live kidney donation during the study period. Surgical mortality from live kidney donation was 3.1 per 10,000 donors (95% confidence interval [CI], 2.0 to 4.6) and did not change over time, despite differences in practice and selection. Long-term risk of death was no higher for live donors than for age- and comorbidity-matched NHANES III participants for all patients and also stratified by age, sex, and race.

Mjoen et al in Norway found that kidney donors are at increased risk of long-term mortality. (4) The investigators identified 1901 kidney donors and compared them with a control group of 32,621 potentially eligible people who had participated in a population-based survey. The kidney transplants occurred between 1963 and 2007 and the median follow-up was 24.9 years. There were 224 (12%) deaths among kidney donors during the study period and 2425 (7%) deaths among controls. The unadjusted hazard ratio (HR) for death by any cause in kidney donors compared with controls was 2.49 (95% CI, 2.13 to 2.91), p<0.001. After adjusting for potential confounding variables, risk of mortality remained elevated among donors (HR=1.48, 95% CI, 1.17 to 1.88), p<0.001.

**Potential contraindications to kidney transplant**

**HIV infection**

In 2001, the Clinical Practice Committee of the American Society of Transplantation proposed that HIV-positive patients, who meet the following criteria, could be considered candidates for kidney transplantation. (5) (These criteria may be extrapolated to other organs.)

- CD4 count >200 cells per cubic millimeter for >6 months
- HIV-1 RNA undetectable
- On stable anti-retroviral therapy >3 months
- No other complications from AIDS (eg, opportunistic infection, including aspergillus, tuberculosis, coccidiosis mycosis, resistant fungal infections, Kaposi’s sarcoma, or other neoplasm).
- Meeting all other criteria for transplantation.
A 2011 review article by European authors stated that there are adequate data suggesting that renal transplantation in adequately selected HIV-positive patients is safe in the short- and medium-term and that patient and graft survival rates are similar to those in HIV-negative patients. (6) Moreover, data do not suggest that immunosuppressive therapy has a negative impact on the course of HIV infection. However, rates of acute rejection after kidney transplantation are higher in HIV-positive patients. In addition, little is known about the management of coinfection with hepatitis C or about the optimal antiretroviral and immunosuppressive regimens. The authors concluded that more studies are needed to address these issues as well as long-term outcomes.

Several case series have evaluated outcomes of kidney transplantation in HIV-positive patients. For example, in 2010, Stock et al published findings of the largest prospective study to date of outcomes following kidney and liver transplantation in HIV-positive recipients. (7) A total of 150 patients underwent kidney transplantation; 102 received kidneys from deceased donors and 48 from living donors. Twenty-eight (19%) of patients were also hepatitis C virus (HCV)-positive. Patients were followed for up to 3 years. The median follow-up of survivors was 1.7 years. The patient survival rate at 1 year was 94.6% (standard deviation [SD]=2.0%) and at 3 years was 88.2% (SD=3.8%). Eleven patients died; the graft was still functioning at the time of death in 8 patients. There were 7 deaths among the 122 HCV-negative patients (6%) and 4 deaths among the 28 HCV-positive patients (14%); the p value for the difference in survival by HCV status was 0.09. Forty-nine of 150 (33%) patients had 67 acute rejection episodes. The cumulative incidence of allograft rejection was 31% (95% CI, 24 to 40) at 1 year and 41% (95% CI, 32 to 52) at 3 years. The time to first acute allograft rejection did not differ significantly among HCV-positive and HCV-negative patients, p=0.36 (exact numbers not reported). Infections requiring hospitalization were reported for 57 of 150 (38%) of patients. Patients who were HCV-positive had a higher rate of serious infection per follow-up year than those who were HCV-negative (0.8 and 0.5, respectively, p=0.02). The authors noted that the rate of rejection was 2 to 3 times higher in this group of HIV-infected patients than in non-HIV-infected patients who participated in a larger study by the research team. They concluded that kidney transplantation is feasible in carefully selected HIV-infected patients and that better strategies are needed for minimizing rejection and for controlling infections in patients who are co-infected with hepatitis C virus.

In 2011, a case-control study from France was published by Mazuecos et al. (8) Outcomes in 20 HIV-positive patients who received kidney transplantation were compared with a matched cohort of 40 HIV-negative patients. Matching was done on a number of variables including type of donor, donor and recipient age, pretransplantation laboratory values, hepatitis B and C status, and treatment at the same center within a short amount of time. There was a mean follow-up of 40.4 months among HIV-positive patients and 39.8 months among HIV-negative patients. Eight (40%) patients in the HIV-positive group and 9 (22.5%) in the HIV-negative group experienced acute rejection; this difference was not statistically significant, p=0.16. There were 4 graft failures (20%) in the HIV-positive group and 2 (5%) in the HIV-negative group; p=0.89. One patient (5%) died in the HIV-positive group, and there were no deaths in the HIV-negative group.

**Hepatitis C infection**

A 2014 meta-analysis by Fabrizi et al identified 18 observational studies comparing kidney transplant outcomes in patients with and without HCV infection. (9) The studies included a total of 133,350 transplant recipients. In an adjusted analysis, the risk of all-cause mortality was significantly higher in HCV-positive versus HCV-negative patients (RR=1.85, 95% CI, 1.49 to 2.31). Risks were elevated in various study subgroups examined by the investigators. When the analysis was limited to the 4 studies from the U.S., the adjusted RR=1.29, 95% CI, 1.15 to 1.44. In an analysis of 10 studies published since 2000, RR=1.84, 95% CI, 1.45 to 2.34. An analysis of disease specific mortality suggested that at least part of the increased risk of mortality among HCV-positive patients may be due to chronic liver disease. In a meta-analysis of 9 studies, the risk of liver disease-related mortality was highly elevated in patients infected with HCV versus uninfected patients: OR=11.6, 95% CI, 5.54 to 24.4.

**Obesity**
In 2014, Pieloch et al published a retrospective review of data from the Organ Procurement and Transplantation Network (OPTN) database. (10) The sample included 6055 morbidly obese patients (ie, body mass index [BMI], 35-40 kg/m²) and 24,077 normal-weight patients who underwent kidney transplant between 2001 and 2006. After controlling for potentially confounding factors, the overall 3-year patient mortality did not differ significantly among obese and normal-weight patients (HR=1.03, 05% CI, 0.96 to 1.12). Similar results were found for 3-year graft failure (HR=1.04, 95% CI, 0.98 to 1.11). In subgroup analyses, obese patients who were nondialysis dependent, nondiabetic, younger, received living-donor transplants, and needed no assistance with daily living activities had significantly lower 3-year mortality rates compared with normal-weight patients who were dialysis dependent, diabetic, had poor functional status, and received a deceased-donor transplant, respectively (P < .01).

In the comparison of mortality in nondiabetic obese and normal-weight patients, the odds ratio (OR) was 0.53, 95% CI, 0.44 to 0.63. A 2013 study by Gill et al examined whether obese patients benefit from kidney transplantation. (11) The study compared outcomes in patients who underwent kidney transplant in the U.S. and those who were on the waiting list. In all BMI categories, risk of mortality at 1 year was significantly lower in patients who underwent transplantation than in those who remained on the waiting list. For example, among patients with a BMI of at least 40 kg/m², who received organs from donors who met standard criteria, HR=0.52, 95 CI, 0.37% to 0.72%. Moreover, among patients with BMI 35 to 39 kg/m² who received organs from standard-criteria donors, HR=0.34, 95% CI, 0.26 to 0.46).

These data suggest that morbid obesity is not associated with an increased risk of adverse outcomes after kidney transplant.

Kidney Retransplant

According to data from the OPTN, rates of 1-year, 3-year, and 5-year survival are similar after a primary kidney transplant and a repeat transplant. (12) For example, for transplants performed between 2002 and 2004, the 1-year survival rate was 91.9% (91.6-% to 92.1%) after primary transplantation and 89.7% (88.8% to 90.5%) after repeat transplantation. Among patients undergoing transplantation between 1997 and 2000, the 5-year survival rate was 72.0% (71.6% to 72.5%) after primary kidney transplantation and 66.9% (65.6% to 68.1%) after repeat kidney transplantation.

In 2009, Barocci et al in Italy reported on long-term survival after kidney retransplantation. (13) There were 100 (0.8%) second transplants of 1302 kidney transplants performed at a single center between January 1983 and June 2007. Among the second kidney recipients, 1-, 5-, and 10-year patient survival was 100%, 96%, and 92%, respectively. Graft survival rates at 1, 5, and 10 years were 85%, 72%, and 53%, respectively.

A 2013 study by Johnston et al compared outcomes in 3509 patients who underwent a preemptive second kidney transplant, defined as transplantation after fewer than 7 days of dialysis following graft failure, to outcomes in 14,075 patients who underwent a nonpreemptive second kidney transplant. (14) Data from the U.S. Renal Data System (USRDS) were reviewed. In the first year after retransplantation, there was a significantly lower risk of acute rejection in patients receiving a preemptive second transplant (12%) compared with those with a nonpreemptive second transplant (16%), p<0.0001. In a multivariate analysis adjusting for demographic differences between groups, there was a significantly lower risk of allograft failure by any cause including death after preemptive second transplants compared with nonpreemptive second transplants (HR=0.88, 95% CI, 0.81 to 0.96).

Summary

Kidney transplant is an accepted treatment of end stage renal disease in appropriately selected patients and thus may be considered medically necessary. Registry and national survey data suggest that live donors of kidneys for transplantation do not have an increased risk of mortality or end stage renal disease (ESRD).
Kidney retransplantation after a failed primary transplant may be considered medically necessary, as national data suggest similar survival rates after initial and repeat transplants.

Kidney transplantation is not medically necessary in patients in whom the procedure is expected to be futile due to comorbid disease or in whom post-transplantation care is expected to significantly worsen comorbid conditions. Case series and case-control data indicate that HIV-infection is not an absolute contraindication to kidney transplant; for patients who meet selection criteria, these studies have demonstrated patient and graft survival rates are similar to those in the general population of kidney transplant recipients.

Practice Guidelines and Position Statements

In 2011, the American Society of Transplant Surgeons, American Society of Transplantation, Association of Organ Procurement Organizations, and the United Network for Organ Sharing (UNOS) issued a position statement recommending the modification of the National Organ Transplant Act of 1984. Their recommendation was that the potential pool of organs from HIV-infected donors be explored. With modern antiretroviral therapy, the use of these previously banned organs would open an additional pool of donors to HIV-infected recipients. The increased pool of donors has the potential to shorten waiting times for organs and decrease the number of waiting list deaths. The organs from HIV infected deceased donors would be used for transplant only with patients already infected with HIV. In 2013 the HIV Organ Policy Equity (HOPE) Act was passed allowing the use of this group of organ donors. (15)

In 2006, the British HIV Association and the British Transplantation Society Standards Committee published guidelines for kidney transplantation in patients with HIV disease. (16) The guidelines recommend that any patient with end stage renal disease with a life expectancy of at least 5 years is considered appropriate for transplantation under the following conditions:

- CD4 >200 cells/mL for at least 6 months
- Undetectable HIV viremia (<50 HIV-1 RNA copies/mL) for at least 6 months
- Demonstrable adherence and a stable HAART [highly active antiretroviral therapy] regimen for at least 6 months
- Absence of AIDS-defining illness following successful immune reconstitution after HAART.

The document lists general and disease-specific exclusion criteria and immunosuppressant protocols. These recommendations are based on level III evidence (observational studies and case reports).

Medicare National Coverage

The Medicare Benefit Policy Manual includes a chapter on end stage renal disease. (17) In a section on identifying candidates for transplantation (140.1), it states, “After a patient is diagnosed as having ESRD, the physician should determine if the patient is suitable for transplantation. If the patient is a suitable transplant candidate, a live donor transplant is considered first because of the high success rate in comparison to a cadaveric transplant. Whether one or multiple potential donors are available, the following sections provide a general description of the usual course of events in preparation for a live-donor transplant.”

References


**Billing Coding/Physician Documentation Information**

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**Additional Policy Key Words**

N/A
Policy Implementation/Update Information

8/1/01 New policy.
8/1/02 No policy statement changes.
8/1/03 No policy statement changes.
8/1/04 Policy statement revised to indicate medullary cystic disease as a medically necessary indication. Added HIV+ status as investigational.
8/1/05 Policy statement revised to remove HIV+ status as investigational.
4/1/06 Added general criteria to the Considerations section.
8/1/06 No policy statement changes.
8/1/07 No policy statement changes.
8/1/08 No policy statement changes.
8/1/09 No policy statement changes.
8/1/10 No policy statement changes.
8/1/11 Not medically necessary statement added specifying criteria indicating absolute contraindications to kidney transplantation.
8/1/12 No policy statement changes.
8/1/13 Contraindications combined (absolute and relative) and moved to Considerations section. Statement added that kidney retransplant after a failed primary kidney transplant may be considered medically necessary.
8/1/14 Statement added that kidney transplantation is considered investigational in all other situations, previously said it was not medically necessary.

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