## Kidney Transplant

<table>
<thead>
<tr>
<th>Type:</th>
<th>Medical Necessity/Not Medical Necessity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy Specific Section:</td>
<td>Transplant</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Original Policy Date:</th>
<th>July 1, 2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effective Date:</td>
<td>July 1, 2011</td>
</tr>
</tbody>
</table>

### Definitions of Decision Determinations

**Medically Necessary:** A treatment, procedure or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

**Investigational/Experimental:** A treatment, procedure or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

**Split Evaluation:** Blue Shield policy review can result in a Split Evaluation, where a treatment, procedure or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

### Description

A kidney (renal) transplant involves the surgical removal of a kidney from a cadaver, living-related, or living-unrelated donor and transplantation into the recipient. Kidney transplant has become the treatment of choice for most patients with end-stage renal disease (ESRD). Studies show that kidney transplantation prolongs patient lifespan relative to dialysis, across most age groups and etiologies of ESRD.
Policy

Kidney transplant with either a living or cadaver donor is considered **medically necessary** for carefully selected candidates with no absolute contraindications (listed below) and one of the following:

- Already on hemodialysis or continuous ambulatory peritoneal dialysis support
- A glomerular filtration rate (GFR) of less than 30 milliliters/minute/1.73 meter squared (30 mL/min/1.73 m²) with any condition that results in end-stage renal disease (see Policy Guideline)

Kidney transplantation is **not medically necessary** in patients with any of the following absolute contraindications:

- Known current malignancy, including metastatic cancer
- Recent malignancy with a high incidence of recurrence
- Untreated systemic infection making immunosuppression unsafe, including chronic infection
- Other irreversible end-stage disease not attributed to kidney disease
- Active human immunodeficiency virus (HIV) disease unless all of the following exist:
  - Cluster of differentiation 4 (CD4) count > 200 cells per cubic millimeter for > six months
  - HIV-1 Ribonucleic acid (RNA) undetectable
  - On stable anti-retroviral therapy > three months
  - No other complications from acquired immune deficiency syndrome (AIDS) (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidiosis mycosis, resistant fungal infections, Kaposi's sarcoma, or other neoplasm)
  - Meet all other criteria for kidney transplantation

Policy Guideline

**Relative Contraindications to Kidney Transplantation:**

- History of cancer with a moderate risk of recurrence
- Systemic disease that could be exacerbated by immunosuppression
- Psychosocial conditions or chemical dependence affecting the ability to adhere to therapy
- Lack of adequate cardiopulmonary reserve

The etiology of ESRD includes, but is not limited to, any of the following conditions associated with ESRD:

- Acute tubular necrosis
- Amyloid disease
- Analgesic nephropathy with medullary necrosis
- Anti-glomerular base-membrane disease
• Chronic pyelonephritis
• Cortical necrosis
• Cystinosis
• Diabetic nephropathy
• Focal glomerulosclerosis
• Fabry's disease
• Glomerulonephritis
• Gout nephritis
• Heavy metal poisoning
• Hemolytic uremic syndrome
• Henoch-Schurpura
• Horseshoe kidney
• Hypertensive nephrosclerosis
• Immunoglobulin A (IgA) nephropathy (also known as Berger's disease)
• Medullary cystic disease
• Myeloma in remission
• Nephritis
• Nephrocalcinosis
• Obstructive uropathy
• Oxalosis
• Polyarteritis
• Polycystic kidney disease
• Renal aplasia or hypoplasia
• Renal artery or vein occlusion
• Renal-cell carcinoma
• Systemic lupus erythematosus
• Trauma requiring nephrectomy
• Tuberous sclerosis
• Wegener's granulomatosis
• Wilms' tumor

**Documentation Required for Clinical Review**

- History and physical
- Laboratory report(s)
- Transplant consultation/evaluation report and progress notes

**Post Service**

- Operative report(s)
The materials provided to you are guidelines used by this plan to authorize, modify, or deny care for persons with similar illness or conditions. Specific care and treatment may vary depending on individual need and the benefits covered under your contract. These Policies are subject to change as new information becomes available.

APPENDIX to Kidney Transplant Policy

Prior Authorization Requirements

Clinical Evidence is required to determine medical necessity.

Within five days before the actual date of service, the Provider MUST confirm with Blue Shield that the member’s health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member’s eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should also be directed to the Prior Authorization Department. Please call 1-800-541-6652 or visit the Provider Portal www.blueshieldca.com/provider.

Evidence Basis for the Policy

Rationale

End-stage renal disease (ESRD) is an irreversible decline in kidney function, severe enough to be fatal in the absence of dialysis or transplantation (Levey et al., 2005). It almost always follows chronic kidney failure (CKD), which may exist 10 to 20 years before progression to ESRD. Kidney transplantation is an accepted and successful treatment of ESRD that results from a variety of etiologies, most commonly diabetic nephropathy. Kidney transplantation should be discussed with all patients with irreversible advanced CKD (Bunnapradist & Danovitch, 2007). It is the only treatment of ESRD that allows a lifestyle without dialysis. Candidates for kidney transplantation must pass an extensive evaluation process.

The Kidney Disease Outcomes Quality Initiatives defines CKD according to the presence or absence of markers of kidney damage and the level of kidney function (glomerular filtration rate (GFR)), irrespective of the type of kidney disease. The GFR is the best overall index of kidney function in health and disease. Normal GFR varies according to sex, age, and body size. The GFR in young adults is approximately 120 to 130 milliliters per minute per 1.73 meter-squared.
Glomerular filtration rate estimates using equations (e.g., Modification of Diet in Renal Disease (MDRD) formula) are more accurate than serum creatinine alone (NKF, 2011). Patients with CKD without known contraindications for transplantation should be referred to a transplant program when they approach an estimated GFR of less than or equal to 30 mL/min/1.73 m² (Bolton, 2003; Bunnapradist & Danovitch, 2007). Early referral improves the chances of a patient receiving a pre-emptive transplant, especially for patients with a potential living donor.

Pre-emptive transplantation (transplantation performed prior to the need for dialysis) generally leads to better outcomes (increased survival) than transplantation after dialysis is initiated. Time spent on dialysis is a predictor of poorer outcomes from renal transplantation. Pre-emptive transplantation is most often pursued in cases of live donor transplants. Due to the shortage of deceased (cadaveric) donor kidney transplants it is unlikely that pre-emptive transplant is a viable option for recipients of deceased donor kidneys. Patients cannot be listed on the United Network for Sharing (UNOS) waiting list for a deceased donor kidney until their estimated GFR, calculated by the MDRD formula, is less than or equal to 20 mL/min/1.73 m² or there is initiation of chronic maintenance dialysis.

A kidney transplant may involve one or both kidneys if the donor is deceased and only one kidney if the donor is living. In most transplants, only one kidney is transplanted. But, in certain circumstances, particularly if the donor is less than ideal, two kidneys may be transplanted. There is also experimental work being done splitting kidneys prior to transplantation, resulting in two recipients per kidney, but this is still extremely rare in practice (Organ Procurement and Transplantation Network (OPTN), 2011).

Kidney transplantation can be performed by an open surgical approach or laparoscopically. A donor left kidney is usually transplanted to the right iliac fossa, with the renal artery anastomosed end-to-end to the hypogastric artery, and the renal vein end-to-side to the common iliac vein. The ureter is implanted into the bladder and (under special conditions) a ureteroureteral anastomosis or uretero-pyelostomy may be performed. The most important complication that may occur after transplant is rejection of the kidney.

As of late 2010, a total of approximately 93,000 patients were registered on the kidney transplant waiting list at the UNOS in the United States (U.S.) (Axelrod et al., 2010). An insufficient supply of donor organs and graft rejection continue to be challenges and targets of research and innovation.

In a 2009 review, Shrestha described strategies for reducing the renal transplant waiting list including:

- Slowing the progression of chronic kidney disease by addressing risk factors and treating conditions that contribute to the development of ESRD
- Increasing organ donation including providing adequate information on the process and benefits of donation and providing high quality care to potential donors
- Using kidneys from donors who do not fulfill the criteria for brain death
• Improving graft survival and reduce transplant losses, including advances in immunosuppressive and supportive therapies and attention to donor and recipient factors before and after transplant
• Using desensitization protocols in patients with antihuman leukocyte antigen antibodies, matching age, sex, and human leukocyte antigens between donor and recipient
• Lowering the rate of delayed graft function by such methods as hypothermic machine perfusion of transplanted kidneys
• Reducing the incidence of acute rejection and calcineurin inhibitor toxicity
• Identification and treatment of viral infections, and treatment regimens that reduce the risk of post-transplant new-onset diabetes after transplant

The author noted screening donors and recipients for malignancies and early diagnosis and treatment of malignancies, non-adherence to immunosuppressive therapy, and chronic allograft nephropathy remain significant challenges.

Shrestha (2009) reported long-term graft survival for living donor kidney transplantation has been shown to be superior to cadaver transplantation while laparoscopic kidney retrieval has reduced the disincentive for living kidney donation. In 2009, 46.8% of kidney transplantations in the U.S. were performed using organs from living donors (Organ Procurement and Transplantation Network, 2010). Two recent papers reported on mortality and long-term survival and long-term renal consequences in live kidney donors. Segev and colleagues (2010) 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 9,364 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 during the last 15 years despite differences in practice and selection. Surgical mortality was higher in men than women, higher in blacks than whites and Hispanics, and higher in those with hypertension than those without. Long-term risk of death was no higher for live donors than for age- and comorbidity-matched NHANES III participants. All patients were also stratified by age, sex, and race.

Ibrahim et al., (2009) reported on the vital status and lifetime risk of ESRD in 3,698 kidney donors who donated kidneys during the period from 1963 through 2007. In the group of donors who donated between 2003 and 2007, the glomerular filtration rate (GFR) and urinary albumin excretion was also measured, and the prevalence of hypertension and general health status was assessed. The survival of kidney donors was similar to that of controls who were matched for age, sex, and race or ethnic group. End-stage renal disease developed in 11 donors, a rate of 180 cases per million persons per year, as compared with a rate of 268 per million per year in the general population. At a mean of 12.2 years after donation, 85.5% of the subgroup of 255 donors had a GFR of 60 milliliters (mL) per minute per 1.73 meter-squared of body-surface area or higher, 32.1% had hypertension, and 12.7% had albuminuria. Older age and higher body-mass index (BMI), but not a longer time since donation, were associated with both a GFR that was lower than 60 mL per minute per 1.73 meter-squared and hypertension. A longer time since donation, however, was independently associated with albuminuria. Most donors had quality-of-
life scores that were better than population norms, and the prevalence of coexisting conditions was similar to that among controls from the NHANES who were matched for age, sex, race or ethnic group, and BMI.

**Kidney Transplant in Human Immunodeficiency Virus-Positive Patients**

This subgroup of recipients has long been controversial, due to the long-term prognosis for human immunodeficiency virus (HIV) positivity and the impact of immunosuppression on HIV disease. However, some transplant surgeons believe HIV positivity is no longer an absolute contraindication to transplant due to the advent of highly active antiretroviral therapy (HAART), which has markedly changed the natural history of the disease.

In 2001, the Clinical Practice Committee of the American Society of Transplantation proposed that the presence of acquired immune deficiency syndrome (AIDS) could be considered a contraindication to kidney transplant, unless the following criteria were present (Steinman et al., 2001).

- Cluster of differentiation 4 (CD4) count > 200 cells per cubic millimeter (mm$^3$) for > six months
- HIV-1 Ribonucleic acid (RNA) undetectable
- On stable anti-retroviral therapy > three months
- No other complications from AIDS (e.g., opportunistic infection, including aspergillus, tuberculosis, coccidiosis mycosis, resistant fungal infections, Kaposi's sarcoma, or other neoplasm).
- Meeting all other criteria for transplantation

These criteria may be extrapolated to other organs.

In 2006, the British HIV Association and the British Transplantation Society Standards Committee published guidelines for kidney transplantation in patients with HIV disease (Bhagani et al., 2006). The guidelines, which are similar to the 2001 guidelines from the American Society of Transplantation cited above (Steinman et al., 2001), recommended any patient with ESRD with a life expectancy of at least five years was considered appropriate for transplantation under the following conditions:

- CD4 > 200 cells/mm$^3$ for at least six months
- Undetectable HIV viremia (< 50 HIV-1 RNA copies/mL) for at least six months
- Demonstrable adherence and a stable HAART regimen for at least six months
- Absence of AIDS-defining illness following successful immune reconstitution after HAART

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

In 2009 UNOS stated asymptomatic HIV-positive patients should not necessarily be excluded for candidacy for organ transplantation, writing:
A potential candidate for organ transplantation whose test for HIV is positive but who is in an asymptomatic state should not necessarily be excluded from candidacy for organ transplantation, but should be advised that he or she may be at increased risk of morbidity and mortality because of immunosuppressive therapy.

Several case series have been published evaluating outcomes of kidney transplantation in HIV-positive patients. For example, in 2010 Thouzot and colleagues in France published findings from a retrospective multicenter series with 27 HIV-infected patients who had kidney transplantsations. The centers all had the same eligibility criteria which included a CD4 count of at least 200 copies per mm$^3$. All patients were treated by HAART and 21 (78%) received a protease inhibitor; all had an undetectable viral load and mean CD4+ T-cell count of 386 per mm$^3$ at the time of transplantation. Mean follow-up was 29 months and the minimum follow-up was 12 months. After one year, patient survival was 100% and graft survival was 98%. After two years, patient survival and graft survival were 98% and 96%, respectively. Four patients (15%) experienced acute rejection; three of these events occurred within three months of transplantation. Median CD4+T-cell counts remained stable; for example, the median count at 12 months was 569 per mm$^3$.

In 2010, Stock and colleagues published preliminary findings of the largest prospective study to date of outcomes following kidney and liver transplantation in HIV-positive recipients. Patients were recruited from 19 centers in the U.S. Eligibility criteria included:

- CD4+ T-cell counts at least 200 cells per mm$^3$
- Undetectable plasma HIV1 (HIV-1) RNA levels (< 50 copies mm) on ultrasensitive polymerase-chain-reaction assay or < 75 copies per mm on viral-load assay while receiving stable HAART during the 16 weeks before transplantation
- Patients with progressive multifocal leukoencephalopathy, chronic intestinal cryptosporidiosis, primary central nervous system lymphoma and visceral Kaposi’s sarcoma were ineligible
- Patients also had to meet center-specific eligibility criteria

A total of 150 patients underwent kidney transplantation at 19 centers in the U.S.; 102 received kidneys from deceased donors and 48 from living donors. Twenty-eight (19%) of patients were hepatitis C virus (HCV) positive. Patients were followed for up to three years. The median follow-up of survivors was 1.7 years. At the time data were analyzed, 53 patients had completed three years of follow-up. The patient survival rate at one year was 94.6% (standard deviation (SD) = 2.0%) and at three years was 88.2% (SD = 3.8%). Eleven patients died; the graft was still functioning at the time of death in eight patients. There were seven deaths among the 122 HCV-negative patients (6%) and four 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 one year and 41% (95% CI = 32 to 52) at three 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). There was a low rate of HIV disease progression. Two patients had newly diagnosed cutaneous Kaposi’s sarcoma, two had newly diagnosed HIV-associated nephropathy and three patients had other new HIV-related diagnoses. Infections requiring
hospitalization were reported in 57 of 150 (38%) 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 the rate of rejection was two to three 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 kidney transplantation is feasible in carefully selected HIV-infected patients and better strategies are needed for minimizing rejection and for controlling infections in patients who are co-infected with HCV.

In 2011, a case-control study from France was published by Mazuecos and colleagues. Outcomes in 20 HIV-positive patients who received kidney transplantation were compared to 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 nine (22.5%) in the HIV-negative group experienced acute rejection; this difference was not statistically significant, p = 0.16. There were four graft failures (20%) in the HIV-positive group and two (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.

A 2011 review article by European researchers' stated there was adequate data suggesting renal transplantation in adequately selected HIV-positive patients is safe in the short- and medium-term and patient and graft survival rates are similar to those in HIV-negative patients (Trullas et al., 2011). Moreover, data did not suggest immunosuppressive therapy had a negative impact on the course of HIV infection. However, rates of acute rejection after kidney transplantation were higher in HIV-positive patients. In addition, little is known about the management of co-infection 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.

In summary, kidney transplant is an accepted treatment of ESRD in appropriately selected patients and thus may be considered medically necessary. Registry and national survey data suggested live donors of kidneys for transplantation do not have an increased risk of mortality or ESRD. 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-controlled data indicated HIV-infection is not an absolute contraindication to kidney transplant. These studies demonstrated patient and graft survival rates are similar to those in the general population of kidney transplant recipients, for patients who meet selection criteria.

**Benefit Application**

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of
service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program (FEP)) prohibit Plans from denying Food and Drug Administration (FDA) - approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

This Policy relates only to the services or supplies described herein. Benefits may vary according to benefit design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement Policy

<table>
<thead>
<tr>
<th>Type</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>50300</td>
<td>Donor nephrectomy (including cold preservation); from cadaver donor, unilateral or bilateral</td>
</tr>
<tr>
<td></td>
<td>50320</td>
<td>Donor nephrectomy (including cold preservation); open, from living donor</td>
</tr>
<tr>
<td></td>
<td>50323</td>
<td>Backbench standard preparation of cadaver donor renal allograft prior to transplantation, including dissection and removal of perinephric fat, diaphragmatic and retroperitoneal attachments, excision of adrenal gland, and preparation of ureter(s), renal vein(s), and renal artery(s), ligating branches, as necessary</td>
</tr>
<tr>
<td></td>
<td>50325</td>
<td>Backbench standard preparation of living donor renal allograft (open or laparoscopic) prior to transplantation, including dissection and removal of perinephric fat and preparation of ureter(s), renal vein(s), and renal artery(s), ligating branches, as necessary</td>
</tr>
<tr>
<td></td>
<td>50327</td>
<td>Backbench reconstruction of cadaver or living donor renal allograft prior to transplantation; venous anastomosis, each</td>
</tr>
<tr>
<td></td>
<td>50328</td>
<td>Backbench reconstruction of cadaver or living donor renal allograft prior to transplantation; arterial anastomosis, each</td>
</tr>
<tr>
<td></td>
<td>50329</td>
<td>Backbench reconstruction of cadaver or living donor renal allograft prior to transplantation; ureteral anastomosis, each</td>
</tr>
<tr>
<td></td>
<td>50340</td>
<td>Recipient nephrectomy (separate procedure)</td>
</tr>
<tr>
<td></td>
<td>50360</td>
<td>Renal allotransplantation, implantation of graft; without recipient nephrectomy</td>
</tr>
<tr>
<td>Type</td>
<td>Number</td>
<td>Description</td>
</tr>
<tr>
<td>------</td>
<td>--------</td>
<td>-------------</td>
</tr>
<tr>
<td>50365</td>
<td>Renal allotransplantation, implantation of graft; with recipient nephrectomy</td>
<td></td>
</tr>
<tr>
<td>50547</td>
<td>Laparoscopy, surgical; donor nephrectomy (including cold preservation), from living donor</td>
<td></td>
</tr>
<tr>
<td>HCPC</td>
<td>S2152</td>
<td>Solid organ(s), complete or segmental, single organ or combination of organs; deceased or living donor(s), procurement, transplantation, and related complications; including: drugs; supplies; hospitalization with outpatient follow-up; medical/surgical, diagnostic, emergency, and rehabilitative services, and the number of days of pre and posttransplant care in the global definition</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD9 Procedure</th>
<th>Procedure</th>
<th>All Diagnoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>55.51</td>
<td>Nephroureterectomy</td>
<td></td>
</tr>
<tr>
<td>55.54</td>
<td>Bilateral nephrectomy</td>
<td></td>
</tr>
<tr>
<td>55.69</td>
<td>Other kidney transplantation</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD9 Diagnosis</th>
<th>All Diagnoses</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Place of Service</th>
<th>All Places of Service</th>
</tr>
</thead>
</table>

**Tables**

**Definitions**

**Definitions**

N/A

**Index / Cross Reference of Related BSC Medical Policies**

The following Medical Policies share diagnoses and/or are equivalent BSC Medical Policies:
• Allogeneic Pancreas Transplant

**Key / Related Searchable Words**

N/A

**References**


Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

<table>
<thead>
<tr>
<th>Effective Date</th>
<th>Action</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>7/1/2011</td>
<td>New policy</td>
<td>Medical Policy Committee</td>
</tr>
</tbody>
</table>

The materials provided to you are guidelines used by this plan to authorize, modify, or deny care for persons with similar illness or conditions. Specific care and treatment may vary depending on individual need and the benefits covered under your contract. These Policies are subject to change as new information becomes available.