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Uterus Transplantation for Absolute Uterine Factor Infertility

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Related Policies (if applicable)
SUR701.033 Laparoscopic, Percutaneous and Transcervical Techniques for Uterine Fibroid Myolysis

Disclaimer

Carefully check state regulations and/or the member contract.
Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For Texas ONLY: For policies (IFM, Student, Small Group, Mid-Market, Large Group, fully insured Municipalities/Counties/Schools, State Employee Plans, PPO, HMO, POS) delivered, issued for delivery, or renewed on or after January 1, 2024, TIC Chapter 1380 (§§ 1380.001 – 1380.003 [SB 1040 Human Organ Transplant]) prohibits coverage of a human organ transplant or post-transplant care if the transplant operation is performed in China or another country known to have participated in forced organ harvesting; or the human organ to be transplanted was procured by a sale or donation originating in China or another country known to have participated in forced organ harvesting. The commissioner of state health services may designate countries who are known to have participated in forced organ harvesting. Forced organ harvesting is defined as the removal of one or more organs from a living person by means of coercion, abduction, deception, fraud, or abuse of power or a position of vulnerability.

Coverage

Uterus transplantation for absolute uterine factor infertility **is considered experimental, investigational and/or unproven.**

Policy Guidelines

None.

Description

Absolute uterine factor infertility is a condition in which an individual is unable to achieve pregnancy due to an absent or non-functioning uterus. Uterus transplantation may present a childbearing option that is an alternative to existing family planning pathways, including adoption, foster parenting, and gestational carrier pregnancy. Uterus transplantation is a complex, multi-stage process involving a living or deceased donor, recipient, and genetic partner.

Absolute Uterine Factor Infertility

Absolute uterine factor infertility (AUFI) refers to infertility that is attributable to an absent or non-functional uterus due to congenital, surgical, anatomical, or acquired factors that prevent embryo implantation and term pregnancy. AUFI is estimated to impact 1 in 500 females of childbearing age. (1, 2)

Uterine agenesis or Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome results in the congenital absence of the uterus or presence of a rudimentary solid bipartite uterus. MRKH syndrome accounts for less than 3% of all müllerian malformations with an estimated prevalence of 1 in 4500 females. (3, 4) Individuals with MRKH syndrome type I present with 2 kidneys and are considered ideal candidates for uterine transplantation. Individuals with MRKH syndrome type II presenting with a single kidney have a higher risk of medication-induced nephrotoxicity and associated obstetric complications (e.g., severe preeclampsia). (5)

Hysterectomy is the most common cause of acquired AUFI, with 240,000 procedures taking place in females under age 44 in the United States. (6) In one clinical trial screening study of 239 individuals at the Cleveland Clinic, indications for uterus transplantation included prior hysterectomy (64%) and congenital anomalies (32%). Among individuals with prior hysterectomy, 50% were performed for benign indications, 25% for malignancy, and 25% for obstetric complications. (7)

Uterus Transplantation

Uterus transplantation may provide a unique fertility restoration option for individuals desiring to carry and birth a child. (8) Uterus transplantation is a complex, multi-stage process involving a living or deceased donor, recipient, and genetic partner. Once screening and consent is established for all involved parties, in-vitro fertilization is performed prior to transplantation to ensure fertilization and normal embryo development. (9) The transplantation surgery involves radical hysterectomy in the donor to ensure long vascular pedicles for transplantation; (10) however, several cases of robot-assisted laparoscopic approaches have been reported. (11, 12) An advantage of uterus procurement in a deceased donor involves freedom to transect ureters,

but this convenience is balanced by the potential for prolonged uterus ischemic time. (13) The surgical approach in the recipient is dictated by underlying pelvic anatomy which may be impacted by AUFI etiology. For example, in individuals with Asherman syndrome, a traditional total hysterectomy must first be performed in the recipient. Immunosuppression is initiated at the time of transplantation and protocol and for-cause cervical biopsies enable monitoring for organ rejection. (14, 15) After 6 to 12 months of immunosuppression, embryo transfer, pregnancy, and cesarean delivery may follow. When childbearing has been deemed complete, the transplanted uterus is removed to avoid lifelong immunosuppression. Thus, uterus transplantation is the first form of organ transplantation intended to be temporary. (1, 9)

The first human uterus transplant was performed in 2000 in Saudi Arabia with a 46-year-old living donor and a 26 year old recipient with acquired AUFI due to hysterectomy for prior post-partum hemorrhage. Due to the development of acute vascular thrombosis at 3 months post-transplant, graft hysterectomy was required. (16) The first successful live birth occurred in 2014 in Sweden in a 35 year old recipient with MRKH syndrome via a living, 61-year-old, 2-parous donor. The recipient was admitted with preeclampsia at 31 weeks, and a healthy male child was born 5 days later via cesarean delivery. (17) The first live birth in the United States occurred in 2017 in a 29-year-old recipient with MRKH syndrome via a living, 32-year-old, 2-parous donor. (18) As of May 2024, 48 uterus transplants resulting in 33 live births have occurred in the United States. (19)

Literature has explored the implications of uterus transplantation in transgender women, identifying several theoretical medical issues in genetic males meriting further investigation. These include creation of adequate de novo uterine vascularization, administration of appropriate hormone replacement therapy, and placement of the donor uterus in a nongynecoid pelvis. (20, 21)

Regulatory Status

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

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

Restorative or life-enhancing uterine vascularized composite allograft (VCA) procurement and transplantation falls under the oversight of the Organ Procurement and Transplantation Network (OPTN). (22)

Rationale

Medical policies assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Due to the nature of absolute uterine factor infertility (AUFI), there are no RCTs directly comparing uterus transplant with alternatives. Systematic reviews are based on case series. Studies comparing surgical technique, infection prophylaxis, and immunosuppressive regimens are not germane to this medical policy.

Uterus Transplantation

Clinical Context and Therapy Purpose

The purpose of uterus transplantation in individuals who have AUFI is to provide a unique childbearing option that is an alternative to or a desired improvement on existing family planning pathways.

The following PICO was used to select literature to inform this policy.

Populations

The relevant population of interest is individuals with AUFI due to an absent or non-functioning uterus. Most congenital cases of uterine agenesis are due to Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome. Individuals with uterine factors contributing to, but not exclusively causing, infertility are generally not considered candidates for uterus transplantation unless established medical or surgical therapeutic options (e.g., hysteroscopic adhesiolysis, myomectomy) have failed. These factors may include müllerian malformations, intrauterine adhesions or Asherman syndrome, radiation injury, poor endometrial receptivity, or uterine leiomyoma(s) of submucosal or intramural type. Most acquired cases of AUFI are due to prior hysterectomy for malignancy, obstetric complications, or uterine fibroids.

Interventions
The therapy being considered is uterus transplantation. Uterus transplantation is a complex, multi-stage process involving a living or deceased donor, recipient, and genetic partner. Uterus transplantation is the first organ transplantation procedure intended to be temporary, concluding with graft hysterectomy to avoid the need for lifelong immunosuppression once childbearing is deemed complete. Pregnancy in the transplanted uterus is achieved through in-vitro fertilization (IVF) and embryo transfer.

Comparators
The relevant comparators are alternative family planning pathways, such as adoption, foster parenting, or gestational carrier pregnancy.

Outcomes
The general outcomes of interest are health status measures, perinatal outcomes, quality of life, treatment-related morbidity, and treatment-related mortality. Benefits and harms should be considered for the donor, recipient, developing fetus, and newborn. Several years of follow-up may be required to fully observe outcomes through all stages of the procedure from procurement through graft removal.

In 2020, the United States Uterus Transplant Consortium issued guidelines for standardized nomenclature and reporting in uterus transplantation trials, identifying 7 progressive stages with milestones of success: 1) technical, 2) menstruation, 3) embryo implantation, 4) pregnancy, 5) delivery, 6) graft removal, and 7) long-term follow-up. (23)

Primary outcomes of interest include recipient posttransplant survival, graft survival, and the transplant success rate, defined as the delivery of a child per transplanted recipient reported at 2-year intervals for the duration of the transplant. Secondary outcomes of interest for recipients include onset of menstruation or withdrawal bleeding, clinical pregnancy, failed embryo transfer, miscarriage, rejection episode(s), stricture, acute kidney injury, adjusted live birth rate, preeclampsia, malignancy, metabolic wellness, health of the newborn, and health of the child. The primary outcome of interest for living uterus donors is patient survival at 1 and 2 years after donation. Secondary outcomes for the living donor include complications (e.g., ureteral complications), hospitalizations, and adverse renal events.

<u>Study Selection Criteria</u>
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Consistent with a 'best available evidence approach,' within each category of study design, studies with larger sample sizes and longer durations were sought.

- Studies with duplicative or overlapping populations were excluded.

Systematic Reviews

Brannstrom et al. (2021) published a systematic review of all published clinical uterus transplantation data and major interim results from 2000 through 2019. (1) Of 62 uterus transplants identified for the review, the overall technical success rate defined as subsequent regular menstruation, was 76%. Technical success rates for living donors (LD) and deceased donor (DD) procedures were 78% and 64%, respectively. Rates of serious postsurgical complications were 18% for living donors and 19% for recipients. Most uterus transplantation procedures to date have involved LD (51/62; 82%). Complications in LD have included ureteric laceration, urinary bladder hypotonia, unplanned bilateral oophorectomy, vaginal dehiscence, fecal impaction, and unilateral pyelonephritis and hydronephrosis. Postoperative complications in recipients have included vaginal anastomotic stenosis and treatable episodes of minor to severe graft rejection.

The cumulative live birth rate per transplant attempt, and per surgically successful uterus transplant is estimated to be >60% and >80%, respectively, as based on 24 published live birth accounts from interim data. High rates of preterm birth (19/24; 80%) and respiratory distress syndrome in the newborn (9/24; 38%) have been observed across cases. Obstetric complications have included preeclampsia, gestational hypertension, and several cases of placenta previa and gestational diabetes. Newborns had an Apgar score of 8 or higher at 5 minutes. One minor malformation in a female newborn involving an anteriorly caudally displaced urethra was reported, which was surgically corrected at 11 months. The reviewers concluded that "the modest success rate and the fairly high complication rate among [LD], indicate that further research and development under strict governance are needed before this option should be widely offered."

Escandon et al. (2022) published a systematic review summarizing data on uterine transplantation from 1995 through November 2020 from PubMed, Cochrane Evidence-Based Medicine Reviews, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials (CENTRAL). (24) A total of 64 uterus transplants were included in the review across 40 publications, including 16 case reports, 5 case reports which were part of an observational study, 2 commentaries, 13 prospective observational studies, and 4 reviews. The quality of included studies was assessed by dual reviewers using the Newcastle-Ottawa Scale (NOS) for nonrandomized cohort studies and the Oxford Center for Evidence-Based Medicine (OCEBM) levels of evidence. Sixteen total studies were graded 2b (individual cohort study or low-quality RCT, n=7) or 4 (case series or poor-quality cohort and case-control studies, n=9) on the OCEBM and scores of 2 (n=1), 4 (n=2), 5(n=11) or 6 (n=2) on the NOS with higher scores indicating better quality reporting of patient selection, comparability, and exposure. No overall assessment of the quality of evidence was provided.

Overall, a total of 75% (48/64) of grafts survived or fulfilled the purpose of transplantation with the majority (41/48; 85%) coming from a LD source. The reasons for transplantation failure included: mechanical occlusion of the uterine vessels (n=1), arterial obstructive disease (n=1),

arterial and or venous thrombosis (n=11), or fungal, viral, or bacterial infections (n=3). A total of 25 live child births from patients with a LD (25/53; 47.2%) and 4 from DDs (4/11; 36.4%) were reported, with 2 recipients having more than 1 newborn (donor type not specified). Complications for recipients included urinary tract infections (UTIs) (n=5), pleural effusion (n=2), retroperitoneal hematoma (n=1), emotional distress (n=1), significant intraoperative blood loss (n=3), bladder injury (n=1), viral respiratory infection (n=2), vaginosis (n=1), vagina anastomosis (n=7), ovarian hyperstimulation syndrome (n=2), persistent post-operative anemia (n=1) and genital tract infections. Mild or borderline rejection episodes were reported in 9 patients, and 1 patient had acute rejection. However, all episodes were successfully controlled with intravenous and oral corticosteroids.

Case Series

Characteristics and interim results from select case series are summarized in Tables 1 and 2. There is an uncertain level of patient overlap between the international registry study by Brännström et al. (2023) (25) and the 2 case series by Fronek et al. (2021) (26) and Brännström et al. (2022) (27), which included individuals treated with uterine transplants at centers in the international registry.

The study by Walter et al. (2024) pools data from the 3 currently active and longest-running clinical research trials on uterine transplantation in the U.S.: NCT02656550 (Testa et al. [2024] [19]; Johannesson et al. [2021) [28]; Putman et al. [2021] [29]) NCT02573415, and NCT03307356. Five-year pooled outcomes data from these 3 key U.S. studies were previously published by Johannesson et al. (2023). (30)

Table 1. Summary of Key Case Series Characteristics

Study	Country (Years)	LD Criteria	Recipient Criteria	Participants
Walter et al. (2024) (31)	United States (2016-2023)	NR	Women with AUFI and intact native ovaries and of childbearing age 20 to 35, negative history of or prior vaccination for HPV, and meets physiological criteria	Median age, 31±4.7 years; 29 MRKH type I or II; 2 prior hysterectomies for leiomyoma(s); Mean donor age, 31.5±7.6 for DD and 37.7±6.5 for LD; 19/31 (61%) LD UTx; 12/31 (29%) DD UTx
Fronek et al. (2021) (26)	Czech Republic (2016-2018)	Female 18 to 60 years of age, ≤4	Female 18 to 40 years of age, AUFI based on	Mean recipient age, 28±3 years; 9 MRKH type I;

		childbirths, ≤1 cesarean section, good general health	congenital or acquired uterus absence, desire for a child, having a male partner, and good general health	1 MRKH type II; Mean donor age, 46±14 years; 5 LD UTx (all related); 5 DD UTx; 5 postmenopausal; 2 nulliparous
Brannstrom et al. (2022) (27)	Sweden (2016-2021)	NR	Females with AUFI <38 years of age, BMI <30, without systemic or psychiatric illness	Mean recipient age, 31.5±3.9; 8 (89%) MRKH type I or II; Mean donor age, 53±7; 9 LD UTx (all related)
Brannstrom et al. (2023) (25)	International Registry (Sweden, China [2 centers]), Czech Republic, Brazil, Germany, Serbia, France, Belgium, Lebanon, Mexico, Spain, and Italy) (2012-2020)	Female with at least 1 normal pregnancy, BMI <28, no serious systemic psychiatric illness, and completion of childbearing	Female of fertile age (generally <39 years of age), BMI <28 and absent overt systemic or psychiatric illness.	Mean recipient age, 29 years (range 22 to 38); 44 (98%) MKRH type I or II; 1 (2%) prior hysterectomy; Mean donor age, NR; 33 LD Utx (all related); 10 DD UTx
Wilson et al. (2023) (32)	United States (2016-2019)	NR	Female 20 to 35 years of age, diagnosis of AUFI with intact native ovaries, BMI ≤30, systemic or active infection, history of cancer in previous 5 years, history of solid organ or bone marrow transplant, history of or prior vaccination for HPV, no history of	Mean recipient age, 31 years (range 20 to 35); 13 (93%) MRKH; 1 (7%) prior hysterectomy

			smoking or drug abuse in previous year, meets physiological criteria	
Javholm et al. (2024) (33)	Sweden (2012-2013)	NR	Female 32 to 43 years of age, with congenital uterine absence or hysterectomy due to cervical cancer	Recipient age range, 32 to 43 years; 31 (94%) MRKH type I or II; 8 (89%) congenital uterine absence; 1 (11%) prior hysterectomy for cancer; 9 (100%) LD UTx
Testa et al. (2024) (19)	United States (2016-2019)	Female between 25 and 65 years of age with at least 1 prior term live birth with no relevant medical or psychological comorbidities	Female 20 to 40 years of age with AUFI and at least 1 functioning ovary	Mean recipient age, 30 (range, 20 to 36); 18 (90%) MKRH syndrome; 2 (10%) prior hysterectomy; Mean donor age, 37 (range, 30 to 56); 18 LD Utx; 2 DD UTx

AUFI: absolute uterine factor infertility; BMI: body mass index; DD: deceased donor; HPV: human papillomavirus; LD: living donor; MRKH: Mayer-Rokitansky-Küster-Hauser syndrome; NR: not reported; UTx: uterus transplant.

Table 2. Summary of Key Case Series Results

Study	Survival	Embryo Transfers, total (range)	Clinical Pregnancy, total (n)	Live Births, total (n)	Live Birth Success Rate	Complications
Walter et al. (2024) (31)	Graft: 23/31	72 (1 to 9)	NR	25 (21); 16 LD and 9 DD	Overall: 35% per embryo transfer; 57% after the first transfer	Acute rejection, gestational hypertension, preeclampsia, gestational diabetes

					and 74% after the second transfer	mellitus, placenta previa, preterm delivery
Fronek et al. (2021) (26)	Graft: 7/10 (70% at 1 year); Recipient: 10/10 (100% at 2 years)	40 (4 to 11)	7 (5)	3 (3); 2 LD and 1 nulliparous DD	Overall: 30%; With surgical success: 43%	Vaginal stenosis, leukopenia, UTI, acute rejection, CMV replication, graft HSV infection, *C. difficile* infection; HLA mismatch, CKD
Brannstrom et al. (2022) (27)	Graft: 7/9 (78% at 4 years); Recipient: 9/9 (100% at 4 years)	46 (1 to 11)	15 (7)	9 (6); 6 LD	Overall: 66.7%; With surgical success: 86%	Acue rejection, anxiety, depression, preeclampsia, respiratory distress syndrome
Branstrom et al. (2023) (25)	Graft: 26/39 (67% at 7 mos)	32 (71% underwent embryo transfer)	NR	19 (16); 14 LD and 2 DD	With surgical success: 40%	Acute rejection, arterial hypertension, cholestasis, elevated creatine, gestational diabetes, gestational hypertension, hematologic cytopenia, opportunistic infection, premature rupture of membranes, subchorionic hematoma

Wilson et al. (2023) (32)	Graft: 14/21 (67% at 1 mo); 13 LD and 1 DD	NR	23 (14)	14 (12)	Overall: 57%; With surgical success: 86%	Acute rejection, CMV viremia, gestational diabetes, gestational hypertension, nausea, opportunistic infection, preeclampsia, pre-pregnancy hypertension, renal toxicity, UTI, vomiting
Javholm et al. (2024) (33)	Graft 7/9 (78% at 3 mo); 9 LD	NR	NR	8 (6)	NR	Median at baseline; year 5 SF-36 PCS: 57.1; 56.9 SF-36 MCS: 54.1; 54.4 HADSA: 3; 1 HADSD: 0; 0 DAS: 131; 115
Testa et al. (2024) (19)	Graft: 14/20 13 LD and 1 DD	Median, 1 (range, 1 to 9)	Clinical pregnancy rate per embryo transfer, 0.52	16 (14)	Overall live birth rate/embryo transfer: 43% Live births by embryo transfer count: 7 (1st transfer), 2 (2nd), 5 (≥3rd)	Acute rejection, infection, vaginal stricture, gestational diabetes and hypertension, preeclampsia, insufficient cervix, preterm labor, placenta previa

CKD: chronic kidney disease; CMV: cytomegalovirus; DAS: dyadic adjustment scale; DD: deceased donor; HADSA: hospital anxiety and depression scale - anxiety; HADSD: hospital anxiety and depression scale - depression; HLA: human leukocyte antigen; HSV: herpes simplex virus; LD: living donor; MRKH: Mayer-Rokitansky-Küster-Hauser syndrome; Mo: months; NR: not reported; SF-36 MCS: short-form 36 mental

component summary; SF-36 PCS: short-form 36 physical component summary; UTI: urinary tract infection.

Section Summary: Uterus Transplantation

Case series of uterus transplantation for AUFI have predominantly enrolled individuals with MRKH syndrome type I. Two systematic reviews of interim trial data have reported live birth success estimates exceeding 60% overall and 80% among transplant attempts with surgical success. Slightly higher technical success rates have been reported for living donor compared to deceased donor procedures (78% vs. 64%, respectively). Rates of serious complications are high among both recipients (19%) and living donors (18%). High rates of preterm birth (80%) and episodes of acute respiratory distress syndrome in the newborn have been reported. Long-term health outcomes in children born via uterus transplantation and recipients following graft hysterectomy continue to accumulate in ongoing trials.

Summary of Evidence

For individuals with absolute uterine factor infertility (AUFI) who receive uterus transplantation, the evidence includes 2 systematic reviews and several case series. Relevant outcomes are health status measures, perinatal outcomes, quality of life, treatment-related morbidity, and treatment-related mortality. Two systematic reviews found similar surgical success rates of 64% for deceased donor procedures and 78% for living donor procedures. These reviews reported 24 to 29 live births, and it was estimated that the overall live birth success rate exceeded 80% among surgically successful transplants. Complications have been reported in 19% of recipients and 18% of living donors. High rates of preterm birth (80%) and episodes of acute respiratory distress syndrome in newborns have been reported. Data for individuals with acquired AUFI are lacking. Further study is necessary to increase success rates, decrease complications and preterm births, and assess long-term outcomes in recipients and their children. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Practice Guidelines and Position Statements

American College of Obstetricians and Gynecologists

In 2018 (reaffirmed 2024), the American College of Obstetricians and Gynecologists (ACOG) Committee on Adolescent Health Care issued a Committee Opinion (Number 728) on the diagnosis, management, and treatment of müllerian agenesis. (34) Regarding future fertility options, the opinion states that while live births have resulted from uterine transplantation, "given limited data, this procedure currently is considered experimental and is not widely available."

American Society for Reproductive Medicine

In 2018, the American Society for Reproductive Medicine (ASRM) issued a position statement recognizing uterus transplantation as the first successful medical treatment for absolute uterine factor infertility, emphasizing its experimental nature. (35) The statement recommends that the procedure should be performed within an Institutional Review Board-approved research protocol, with recommendations for the composition of "well-coordinated and

multidisciplinary" uterus transplantation teams and suggested recipient inclusion and exclusion criteria.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this policy are listed in Table 3.

Table 3. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT02573415	Uterine Transplantation for the Treatment of Uterine Factor Infertility	10	Oct 2025
NCT03252795	Uterus Transplantation From a Multi-organ Donor: A Prospective Trial	20	Dec 2027
NCT04244409	INvestigational Study Into Transplantation of the Uterus (INSITU)	10	Feb 2024
NCT03689842	Feasibility Study of Uterine Transplantation From Living Donors in Terms of Efficacy and Safety in Patients With Mayer-Rokitansky-Küster-Hauser Syndrome (MRKH)	20	Dec 2034
NCT04026893	Deceased Uterine Transplant in Absolute Uterine Infertility	250	Oct 2025
NCT03277430	Uterus Transplantation From Live Donors and From Deceased Donors - Clinical Study (UTxLD/DBD)	20	Dec 2025
NCT03581019	Uterus Transplantation From Deceased Donor - Gothenburg III	8	Dec 2023
NCT04314869	Feasibility Study of Uterus Transplantation Procedure From a Live Donor Obtaining the Graft by Laparoscopy	10	Dec 2025
NCT02656550	Uterine Transplantation and Pregnancy Induction in Women Affected by Absolute Uterine Infertility	20	Jan 2026
NCT03307356	The University of Pennsylvania Uterus Transplant for Uterine Factor Infertility Trial (UNTIL)	5	Jul 2029
NCT05263076	Uterine Transplantation and Pregnancy Induction in Women Affected by Absolute Uterine Factor Infertility	10	Dec 2030

NCT05646992	OPRTUNTI: Offering Potential for Reproduction Through Transplantation of Uterus iN the Treatment of Infertility	40	Feb 2033
NCT05726305	Transplantation of Uterus for Uterine infertiLIty From Living Donor or Deceased Donor (TULIPE)	16	Dec 2037
Unpublished			
NCT02741102	Uterine Transplant in Absolute Uterine Infertility (AUIF)	10	Jan 2023 (unknown status)

NCT: national clinical trial; No: number.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	0664T, 0665T, 0666T, 0667T, 0668T, 0669T, 0670T
HCPCS Codes	None

*Current Procedural Terminology (CPT®) ©2025 American Medical Association: Chicago, IL.

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision	
Date	**Description of Change**
05/01/2026	New medical document. Uterus transplantation for absolute uterine factor infertility is considered experimental, investigational and/or unproven.