

Missouri Care

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WellCare | HERITAGE HEALTH

Thymus Transplant:
Policy Number: CP.MP.189

Last Review Date: 06/20

APPLICATION STATEMENT

The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

DISCLAIMER

The Clinical Coverage Guideline (CCG) is intended to supplement certain standard WellCare benefit plans and aid in administering benefits. Federal and state law, contract language, etc. take precedence over the CCG (e.g., Centers for Medicare and Medicaid Services [CMS] National Coverage Determinations [NCDs], Local Coverage Determinations [LCDs] or other published documents). The terms of a member's particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member's benefit plan may contain specific exclusions related to the topic addressed in this CCG. Additionally, CCGs relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. Providers are responsible for the treatment and recommendations provided to the member. The application of the CCG is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations, and any state-specific Medicaid mandates. Links are current at time of approval by the Medical Policy Committee (MPC) and are subject to change. Lines of business are also subject to change without notice and are noted on www.wellcare.com. Guidelines are also available on the site by selecting the Provider tab, then "Tools" and "Clinical Guidelines".

BACKGROUND

DiGeorge syndrome (DGS) is a disorder in which there is a defect in the development of the pharyngeal pouch system. The syndrome is most commonly caused by a chromosomal deletion at 22q11.2. DGS includes many signs and symptoms with the classic three being congenital cardiac anomalies, underdevelopment of the thymus, and hypocalcemia due to parathyroid hypoplasia. Other common findings in DGS patients include, cleft lip or palate, club feet, single kidney, esophageal atresia, butterfly vertebra, rib abnormalities, and laryngomalacia.² Thanks to medical advances, improved palliative cardiac repair, and medical management of immunodeficiency, infant mortality in DGS is now approximately 4%.³

Thymus Transplantation – A study published in Clinical Immunology followed the transplantation of postnatal allogeneic cultured thymus tissue in sixty subjects under the age of 2 years with complete DGS. The study participant survival rate was over 70% and naïve T cells developed 3–5 months after transplantation. The transplant recipients were able to discontinue antibiotic prophylaxis, and immunoglobulin replacement. Immunosuppression was used in a subset of subjects and was discontinued when naïve T cells developed.⁸

Another study showed that 43 out of 60 infants treated by cultured postnatal thymic transplantation were alive at the time of reporting. 15 out of 17 of the deaths has occurred within 12 months of the transplant and most were due to infections, with higher risk for mortality-related infection associated with tracheostomies or mechanical ventilation. One of the deaths was related to complications of calcium therapy. For patients with atypical DGS, immunosuppressive therapy was given prior to transplantation to increase the chances of success for tissue engraftment.¹²

Duke University Medical Center Thymus Transplantation

Currently in the United States, thymus transplantation with RVT-802 is performed under a Biological License Application (BLA) with the Food and Drug Administration (FDA). Treatment can be received as part of a safety and access protocol (Pro00025966) or an expanded access protocol (Pro00051692) at Duke University Medical center and participants must be enrolled in a Phase I/II safety and efficacy study for the treatment of complete DiGeorge anomaly. Eligible participants undergo thymus transplantation and biopsy. Immune function testing is continued for one year post-transplantation.¹

POSITION STATEMENT

Complete DiGeorge anomaly is a disorder in which a person has no thymus function. Without thymus function, bone marrow stem cells do not develop into T cells, which results in immunodeficiency. Without successful treatment, patients usually die by 2 years of age. Thymus transplantation with and without immunosuppression has resulted in the development good T cell function in complete DiGeorge anomaly subjects.¹

Policy/Criteria

- I. It is the policy of health plans affiliated with Centene Corporation® that thymus transplant (use of RVT-802) requires secondary review, due to limited evidence, when meeting all of the following:
 - A. Complete or “atypical” DiGeorge syndrome with poor thymus function, per medical testing laboratory studies and physical examination, as confirmed by the thymus transplant clinical trial (NCT01220531);
 - B. Immunodeficiency, or severe autoimmunity for which development of naïve T cells would be expected to lead to clinical improvement;
 - C. Flow cytometry and phytohaemagglutinin (PHA) studies are planned to occur twice, once within 3 months of transplantation and once within one month of transplantation. Studies must be performed in a CLIA or CAP certified laboratory, preferably Duke Clinical Immunology Laboratory;
 - D. None of the following contraindications:
 - 1. Malignancy, except for non-melanoma localized skin cancer that has been treated appropriately, a malignancy that has been completely resected, or a treated malignancy determined to have a small likelihood of recurrence and acceptable future risks;
 - 2. Untreatable significant dysfunction of another major organ system unless combined organ transplantation can be performed;
 - 3. Acute medical instability, including, but not limited to, acute sepsis, acute viral respiratory infection, myocardial infarction, and liver failure;
 - 4. Chronic infection with highly virulent and/or resistant microbes that are poorly controlled pre-transplant;
 - 5. Heart surgery conducted less than four weeks prior to the projected transplantation date;
 - 6. Heart surgery anticipated within three months after the proposed time of transplantation;
 - 7. Lack of sufficient muscle tissue to accept a transplant of 2000 mm² surface area/m² body surface area of the recipient;
 - 8. Cytomegalovirus (CMV) infection (CMV PCR result of >500 copies/ml on two consecutive assays or two positive urine cultures) in patients with atypical complete DiGeorge anomaly.

CODING

CPT® Codes	Description
60699	Unlisted procedure, endocrine system
81405	Molecular pathology procedure level 6
81422	Fetal chromosomal microdeletion(s) genomic sequence analysis (eg, DiGeorge syndrome, Cri-du-chat syndrome), circulating cell-free fetal DNA in maternal blood
86355	B cells, total count

ICD-10-CM Diagnosis Codes that Support Coverage Criteria

+ Indicates a code(s) requiring an additional character

ICD-10-CM Code	Description
07YM0Z0 – 07YM0Z2	Transplantation of Thymus

Coding information is provided for informational purposes only. The inclusion or omission of a CPT, HCPCS, or ICD-10 code does not imply member coverage or provider reimbursement. Consult the member's benefits that are in place at time of service to determine coverage (or non-coverage) as well as applicable federal/ state laws.

REFERENCES

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REVIEWS, REVISIONS, AND APPROVALS

	Date	Approval Date
Policy adopted from WellCare's HS-265. In I.A, reworded mention of SME and Safety and Review Board to include the clinical trial identifier. Removed requirement that immune criteria are met per trial protocol. Removed the following contraindications, as they were duplicative with added contraindications: unrepaired CHD; uncontrolled infection; HIV infection; heart surgery less than 4 weeks prior to transplant; rejection by surgeon or anesthesiologist as a surgical candidate; ventilator dependence; malignancy. Removed pregnancy as a contraindication. Added the following contraindications: Malignancy with specific exceptions; untreatable significant dysfunction of another major organ system; acute medical instability; chronic infection with highly virulent and/or resistant microbes that are poorly controlled. Shortened background.	06/20	06/20