Clinical Policy: Thymus Transplantation

Reference Number: CP.MP.189 Coding Implications
Last Review Date: 06/20 Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

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 mm^2 surface area/m^2 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.

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]

Coding Implications

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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

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

References

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Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to

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This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.