Clinical Policy: Thymus Transplantation

Reference Number: LA.CP.MP.189 Coding Implications
Last Review Date: 08/2020 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 Louisiana Healthcare Connections 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

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2020, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

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
Converted corporate to local policy.	08/15/2020	

References

1. Thymus transplantation safety-efficacy. In: ClinicalTrails.gov [Internet]. Markert (MD): December 2010 (updated July 19, 2019) Available from: https://clinicaltrials.gov/ct2/show/record/NCT01220531 NLM Identifier: NCT01220531. Accessed June 1, 2020.
2. Seroogy CM. DiGeorge (22q11.2 deletion) syndrome: Clinical features and diagnosis. UpToDate. June 11, 2019. Accessed June 1, 2020.
3. Basset AS, Mcdonald-McGinn DM, Devriendt K, et al. Practical guidelines for managing patients with 22q.11.2 deletion syndrome. J Pediatr. 2011;159(2). doi:10.1016/j.jpeds.2011.02.039.
4. Seroogy CM. DiGeorge syndrome: Pathogenesis, epidemiology, and clinical manifestations. UpToDate. Updated June 7, 2019. Accessed June 1, 2020.
5. Markert ML, Boeck A, Hale LP, et al. Transplantation of thymus tissue in complete DiGeorge syndrome. N Engl J Med. 1999;341:1180-1189. Doi:10.1056/NEJM199910143411603
6. Zemble R, Prak EL, McDonald K, et al. Secondary immunologic consequences in chromosome 22q11.2 deletion syndrome (DiGeorge syndrome/velocardiofacial syndrome). Clin Immunol. 2010;136(3):409-418. doi:10.1016/j.clim.2010.02.007.
7. Bonilla FA, Khan DA, Ballas ZK, et al. Practice parameter for the diagnosis and management of primary immunodeficiency. J Allergy Clin Immunol. 2015 Nov;136(5):1186-120.
8. Markert ML, Devlin BH, McCarthy EA. Thymus Transplantation. Clin Immunol. 2010;135(2):236-246. doi:10.1016/j.clim.2010.02.007.
9. Janda A, Sedlacek P, Mejstrikova E, et al. Unrelated partially matched lymphocyte infusions in a patient with complete DiGeorge/CHARGE syndrome.Pediatr Transplant 2007;11:441-7. doi:10.1111/j.1399-3046.2007.00702.x

10. Land MH, Garcia-Lloret MI, Borsy MS, et al. Long-term results of bone marrow transplantation in complete DiGeorge syndrome. J Allergy Clin Immunol 2007;120:908-15. doi:10.1016/j.jaci.2007.08.048.
11. McGhee SA, Lloret MG, Stiehm ER. Immunologic reconstititution in 22q deletion (DiGeorge) syndrome. Immunol Res. 2009;45(1):37-45. doi:10.1007/a12026-009-8108-7.
12. Seroogy CM. DiGeorge (22q11.2 deletion) syndrome: Management and prognosis. UpToDate. Updated September 9, 2019. Accessed June 1, 2020.
13. Markert ML1, Hummell DS, Rosenblatt HM, et al. Complete DiGeorge syndrome: persistence of profound immunodeficiency. J Pediatr. 1998;132(1).
14. Enzyvant. Pipeline: RVT-802. Enzyvant Therapeutics GmbH. Accessed June 6, 2020. https://enzyvant.com/pipeline/

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. LHCC 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.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom LHCC has no control or right of control. Providers are not agents or employees of LHCC.