

CLINICAL PAYMENT AND CODING POLICY

If a conflict arises between a Clinical Payment and Coding Policy (CPCP) and any plan document under which a member is entitled to Covered Services, the plan document will govern. If a conflict arises between a CPCP and any provider contract pursuant to which a provider participates in and/or provides Covered Services to eligible member(s) and/or plans, the provider contract will govern. "Plan documents" include, but are not limited to, Certificates of Health Care Benefits, benefit booklets, Summary Plan Descriptions, and other coverage documents. BCBSTX may use reasonable discretion interpreting and applying this policy to services being delivered in a particular case. BCBSTX has full and final discretionary authority for their interpretation and application to the extent provided under any applicable plan documents.

Providers are responsible for submission of accurate documentation of services performed. Providers are expected to submit claims for services rendered using valid code combinations from Health Insurance Portability and Accountability Act (HIPAA) approved code sets. Claims should be coded appropriately according to industry standard coding guidelines including, but not limited to: Uniform Billing (UB) Editor, American Medical Association (AMA), Current Procedural Terminology (CPT®), CPT® Assistant, Healthcare Common Procedure Coding System (HCPCS), ICD-10 CM and PCS, National Drug Codes (NDC), Diagnosis Related Group (DRG) guidelines, Centers for Medicare and Medicaid Services (CMS) National Correct Coding Initiative (NCCI) Policy Manual, CCI table edits and other CMS guidelines.

Claims are subject to the code edit protocols for services/procedures billed. Claim submissions are subject to claim review including but not limited to, any terms of benefit coverage, provider contract language, medical policies, clinical payment and coding policies as well as coding software logic. Upon request, the provider is urged to submit any additional documentation.

Immune Cell Function Assay

Policy Number: CPCPLAB028

Version 1.0

Enterprise Medical Policy Committee Approval Date: 1/25/2022

Plan Effective Date: May 1, 2022

Description

BCBSTX has implemented certain lab management reimbursement criteria. Not all requirements apply to each product. Providers are urged to review Plan documents for eligible coverage for services rendered.

Reimbursement Information:

1. Use of an immune cell function assay to monitor and predict immune function after solid organ transplantation **may be reimbursable**.

2. An immune cell function assay **is not reimbursable** for all indications including, but not limited to:
 - a. Management of autologous or allogeneic hematopoietic stem cell transplantation;
 - b. Management of immunodeficiency disorders including human immunodeficiency virus (HIV) and severe combined immunodeficiency disease (SCID);
 - c. Management of or prediction of infection risk in immune mediated disorders including rheumatoid arthritis (RA), multiple sclerosis, and lupus nephritis;
 - d. Testing for urticaria;
 - e. Diagnosis and management of Lyme disease (for example, iSpot Lyme Test).
 - f. Management of inflammatory bowel diseases;
 - g. Monitoring immune response following surgery.

Procedure Codes

Codes
86352

References:

Ashokkumar, C., Gupta, A., Sun, Q., Ningappa, M. B., Higgs, B. W., Mazariegos, G., . . . Sindhi, R. (2009). Allospecific CD154+ T cells identify rejection-prone recipients after pediatric small-bowel transplantation. *Surgery*, 146(2), 166-173. doi:10.1016/j.surg.2009.04.006

Ashokkumar, C., Soltys, K., Mazariegos, G., Bond, G., Higgs, B. W., Ningappa, M., . . . Sindhi, R. (2017). Predicting Cellular Rejection With a Cell-Based Assay: Preclinical Evaluation in Children. *Transplantation*, 101(1), 131-140. doi:10.1097/tp.0000000000001076

AST. (2009). GUIDELINES FOR POST-KIDNEY TRANSPLANT MANAGEMENT IN THE COMMUNITY SETTING. Retrieved from <https://www.myast.org/guidelines-post-kidney-transplant-management-community-setting>

Bonilla, F. A. (2008). Interpretation of lymphocyte proliferation tests. *Ann Allergy Asthma Immunol*, 101(1), 101-104. doi:10.1016/s1081-1206(10)60842-3

Bonilla, F. A., Khan, D. A., Ballas, Z. K., Chinen, J., Frank, M. M., Hsu, J. T., . . . Wallace, D. (2015). Practice parameter for the diagnosis and management of primary immunodeficiency. *J Allergy Clin Immunol*, 136(5), 1186-1205.e1181-1178. doi:10.1016/j.jaci.2015.04.049

Butte, M., & Stiehm, R. (2019). Laboratory evaluation of the immune system - UpToDate. In A. Feldweg (Ed.), *UpToDate*. Retrieved from https://www.uptodate.com/contents/laboratory-evaluation-of-the-immune-system?source=search_result&search=lymphocyte%20mitogen%20response&selectedTitle=2~150

Buttgereit, F., Burmester, G. R., & Brand, M. D. (2000). Bioenergetics of immune functions: fundamental and therapeutic aspects. *Immunol Today*, 21(4), 192-199. Retrieved from <http://dx.doi.org/>

Chiereghin, A., Petrisli, E., Ravaioli, M., Morelli, M. C., Turello, G., Squarzone, D., . . . Lazzarotto, T. (2017). Infectious agents after liver transplant: etiology, timeline and patients' cell-mediated immunity responses. *Med Microbiol Immunol*, 206(1), 63-71. doi:10.1007/s00430-016-0485-7

Chon, W. J., Malone, Andrew, Anglicheau, Dany. (2020). Investigational methods in the diagnosis of acute renal allograft rejection - UpToDate. In UpToDate. Retrieved from <https://www.uptodate.com/contents/investigational-methods-in-the-diagnosis-of-acute-renal-allograft-rejection?source=machineLearning&search=immunoknow&selectedTitle=1~1§ionRank=1&anchor=H3#H3>

Clark, N., & Cotler, S. (2020). Infectious complications in liver transplantation - UpToDate. Retrieved from https://www.uptodate.com/contents/infectious-complications-in-liver-transplantation?search=immuknow&source=search_result&selectedTitle=1~1&usage_type=default&display_rank=1

Costanzo, M. R., Dipchand, A., Starling, R., Anderson, A., Chan, M., Desai, S., . . . Vanhaecke, J. (2010). The International Society of Heart and Lung Transplantation Guidelines for the care of heart transplant recipients. *J Heart Lung Transplant*, 29(8), 914-956. doi:10.1016/j.healun.2010.05.034

Fernandez-Ruiz, M., Kumar, D., & Humar, A. (2014). Clinical immune-monitoring strategies for predicting infection risk in solid organ transplantation. *Clin Transl Immunology*, 3(2), e12. doi:10.1038/cti.2014.3

Humar, A., & Michaels, M. (2006). American Society of Transplantation recommendations for screening, monitoring and reporting of infectious complications in immunosuppression trials in recipients of organ transplantation. *Am J Transplant*, 6(2), 262-274. doi:10.1111/j.1600-6143.2005.01207.x

Intellicyt. (2021). Immune Cell Function Assays. Retrieved from <https://intellicyt.com/applications/immune-cell-function/>

Jo, Y., Lim, J., Kim, Y., Han, K., Min, W. S., & Oh, E. J. (2015). CD4 T-cell function assay using Cylex ImmuKnow and lymphocyte subset recovery following allogeneic hematopoietic stem cell transplantation. *Transpl Immunol*, 33(2), 78-83. doi:10.1016/j.trim.2015.09.001

Kobashigawa, J., Colvin, M., Potena, L., Dragun, D., Crespo-Leiro, M. G., Delgado, J. F., . . . Zuckermann, A. (2018). The management of antibodies in heart transplantation: An ISHLT consensus document. *J Heart Lung Transplant*, 37(5), 537-547. doi:10.1016/j.healun.2018.01.1291

Kotton, C. N., Kumar, D., Caliendo, A. M., Huprikar, S., Chou, S., Danziger-Isakov, L., & Humar, A. (2018). The Third International Consensus Guidelines on the Management of Cytomegalovirus in Solid-organ Transplantation. *Transplantation*, 102(6), 900-931. doi:10.1097/tp.0000000000002191

Kowalski, R. J., Post, D. R., Mannon, R. B., Sebastian, A., Wright, H. I., Sigle, G., . . . Britz, J. A. (2006). Assessing relative risks of infection and rejection: a meta-analysis using an immune function assay. *Transplantation*, 82(5), 663-668. doi:10.1097/01.tp.0000234837.02126.70

- Levine, D. J., Glanville, A. R., Aboyoun, C., Belperio, J., Benden, C., Berry, G. J., . . . Zeevi, A. (2016). Antibody-mediated rejection of the lung: A consensus report of the International Society for Heart and Lung Transplantation. *J Heart Lung Transplant*, 35(4), 397-406. doi:10.1016/j.healun.2016.01.1223
- Ling, X., Xiong, J., Liang, W., Schroder, P. M., Wu, L., Ju, W., . . . He, X. (2012). Can immune cell function assay identify patients at risk of infection or rejection? A meta-analysis. *Transplantation*, 93(7), 737-743. doi:10.1097/TP.0b013e3182466248
- Liu, W., Wang, K., Zhao, Y. H., Song, G. P., Gao, W., & Li, D. H. (2019). Clinical relevance of a CD4(+) T cell immune function assay in the diagnosis of infection in pediatric living-donor liver transplantation. *Exp Ther Med*, 18(5), 3823-3828. doi:10.3892/etm.2019.8003
- Lucey, M. R., Terrault, N., Ojo, L., Hay, J. E., Neuberger, J., Blumberg, E., & Teperman, L. W. (2013). Long-term management of the successful adult liver transplant: 2012 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. *Liver Transpl*, 19(1), 3-26. doi:10.1002/lt.23566
- Monforte, V., Ussetti, P., Castejón, R., Sintes, H., Pérez, V. L., Laporta, R., . . . Gómez-Ollés, S. (2021). Predictive Value of Immune Cell Functional Assay for Non-Cytomegalovirus Infection in Lung Transplant Recipients: A Multicenter Prospective Observational Study. *Archivos de Bronconeumología*. doi:https://doi.org/10.1016/j.arbres.2020.12.024
- Notarangelo, L. D. (2010). Primary immunodeficiencies. *J Allergy Clin Immunol*, 125(2 Suppl 2), S182-194. doi:10.1016/j.jaci.2009.07.053
- Oliveira, J. B., & Fleisher, T. A. (2010). Laboratory evaluation of primary immunodeficiencies. *J Allergy Clin Immunol*, 125(2 Suppl 2), S297-305. doi:10.1016/j.jaci.2009.08.043
- Picard, C., Al-Herz, W., Bousfiha, A., Casanova, J. L., Chatila, T., Conley, M. E., . . . Gaspar, H. B. (2015). Primary Immunodeficiency Diseases: an Update on the Classification from the International Union of Immunological Societies Expert Committee for Primary Immunodeficiency 2015. *J Clin Immunol*, 35(8), 696-726. doi:10.1007/s10875-015-0201-1
- Piloni, D., Magni, S., Oggionni, T., Benazzo, A., Stella, G., Scudeller, L., . . . Meloni, F. (2016). Clinical utility of CD4+ function assessment (ViraCor-IBT ImmuKnow test) in lung recipients. *Transpl Immunol*, 37, 35-39. doi:10.1016/j.trim.2016.04.001
- Ravaioli, M., Neri, F., Lazzarotto, T., Bertuzzo, V. R., Di Gioia, P., Stacchini, G., . . . Pinna, A. D. (2015). Immunosuppression Modifications Based on an Immune Response Assay: Results of a Randomized, Controlled Trial. *Transplantation*, 99(8), 1625-1632. doi:10.1097/tp.0000000000000650
- Rodrigo, E., Lopez-Hoyos, M., Corral, M., Fabrega, E., Fernandez-Fresnedo, G., San Segundo, D., . . . Arias, M. (2012). ImmuKnow as a diagnostic tool for predicting infection and acute rejection in adult liver transplant recipients: a systematic review and meta-analysis. *Liver Transpl*, 18(10), 1245-1253. doi:10.1002/lt.23497

- Sindhi, R., Ashokkumar, C., Higgs, B. W., Levy, S., Soltys, K., Bond, G., . . . Zeevi, A. (2016). Profile of the Pleximmune blood test for transplant rejection risk prediction. *Expert Rev Mol Diagn*, 16(4), 387-393. doi:10.1586/14737159.2016.1139455
- Sottong, P. R., Rosebrock, J. A., Britz, J. A., & Kramer, T. R. (2000). Measurement of T-lymphocyte responses in whole-blood cultures using newly synthesized DNA and ATP. *Clin Diagn Lab Immunol*, 7(2), 307-311. Retrieved from <http://dx.doi.org/>
- Stiehm, R. (2017). Laboratory evaluation of the immune system - UpToDate. In A. Feldweg (Ed.), UpToDate. Retrieved from https://www.uptodate.com/contents/laboratory-evaluation-of-the-immune-system?source=search_result&search=lymphocyte%20mitogen%20response&selectedTitle=2~150
- Vella, J. (2019). Transplantation immunobiology - UpToDate. In D. Brennan (Ed.), UpToDate. Retrieved from https://www.uptodate.com/contents/transplantation-immunobiology?source=search_result&search=organ%20rejection&selectedTitle=2~150#H1
- Wang, Z., Liu, X., Lu, P., Han, Z., Tao, J., Wang, J., . . . Gu, M. (2014). Performance of the ImmuKnow assay in differentiating infection and acute rejection after kidney transplantation: a meta-analysis. *Transplant Proc*, 46(10), 3343-3351. doi:10.1016/j.transproceed.2014.09.109
- Xue, F., Gao, W., Qin, T., Wu, C., Luo, Y., Chen, J., . . . Xia, Q. (2021). Immune cell function assays in the diagnosis of infection in pediatric liver transplantation: an open-labeled, two center prospective cohort study. *Translational pediatrics*, 10(2), 333-343. doi:10.21037/tp-20-256
- Weston, M. W., Rinde-Hoffman, D., & Lopez-Cepero, M. (2020). Monitoring cell-mediated immunity during immunosuppression reduction in heart transplant recipients with severe systemic infections. *Clin Transplant*, 34(3), e13809. doi:10.1111/ctr.13809
- Zhang, W., Zhong, H., Zhuang, L., Yu, J., Xu, X., Wang, W., . . . Zheng, S. (2016). Peripheral blood CD4(+) cell ATP activity measurement to predict HCC recurrence post-DCD liver transplant. *Int J Clin Pract*, 70 Suppl 185(Suppl 185), 11-16. doi:10.1111/ijcp.12811

Policy Update History:

5/1/22	New policy
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