

If a conflict arises between a Clinical Payment and Coding Policy 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. Blue Cross and Blue Shield of TX may use reasonable discretion interpreting and applying this policy to services being delivered in a particular case. Blue Cross and Blue Shield of TX 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 approved code sets. Claims should be coded appropriately according to industry standard coding guidelines including, but not limited to: Uniform Billing Editor, American Medical Association, Current Procedural Terminology, CPT® Assistant, Healthcare Common Procedure Coding System, ICD-10 CM and PCS, National Drug Codes, Diagnosis Related Group guidelines, Centers for Medicare and Medicaid Services National Correct Coding Initiative 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**

**Approval Date:** Sept. 13, 2024

**Plan Effective Date:** Jan. 1, 2025 (Blue Cross and Blue Shield of Texas Only)

## Description

The plan 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

The following is not an all-encompassing code list. The inclusion of a code does not guarantee it is a covered service or eligible for reimbursement.

Codes
81560, 86352, 0018M

## References:

Anglicheau, D., Malone, A., & Chon, W. J. (2023, January 3). Investigational methods in the diagnosis of acute renal allograft rejection.  
<https://www.uptodate.com/contents/investigational-methods-in-the-diagnosis-of-acute-renal-allograft-rejection>

Ashokkumar, C., Gupta, A., Sun, Q., Ningappa, M. B., Higgs, B. W., Mazariegos, G., Fazzolare, T., Remaley, L., Soltys, K., Bond, G., Abu-Elmagd, K., & Sindhi, R. (2009). Allospecific CD154+ T cells identify rejection-prone recipients after pediatric small-bowel transplantation. *Surgery*, *146*(2), 166-173.  
<https://doi.org/10.1016/j.surg.2009.04.006>

Ashokkumar, C., Soltys, K., Mazariegos, G., Bond, G., Higgs, B. W., Ningappa, M., Sun, Q., Brown, A., White, J., Levy, S., Fazzolare, T., Remaley, L., Dirling, K., Harris, P., Hartle, T., Kachmar, P., Nicely, M., O'Toole, L., Boehm, B., . . . Sindhi, R. (2017). Predicting Cellular Rejection With a Cell-Based Assay: Preclinical Evaluation in Children. *Transplantation*, *101*(1), 131-140.  
<https://doi.org/10.1097/tp.0000000000001076>

AST. (2009). GUIDELINES FOR POST-KIDNEY TRANSPLANT MANAGEMENT IN THE COMMUNITY SETTING.  
<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. [https://doi.org/10.1016/s1081-1206\(10\)60842-3](https://doi.org/10.1016/s1081-1206(10)60842-3)

Bonilla, F. A., Khan, D. A., Ballas, Z. K., Chinen, J., Frank, M. M., Hsu, J. T., Keller, M., Kobrynski, L. J., Komarow, H. D., Mazer, B., Nelson, R. P., Jr., Orange, J. S., Routes, J. M., Shearer, W. T., Sorensen, R. U., Verbsky, J. W., Bernstein, D. I., Blessing-Moore, J., Lang, D., . . . Wallace, D. (2015). Practice parameter for the diagnosis and management of primary immunodeficiency. *J Allergy Clin Immunol*, *136*(5), 1186-1205.e1181-1178.  
<https://doi.org/10.1016/j.jaci.2015.04.049>

Butte, M. J. (2023, February 2). Laboratory evaluation of the immune system.  
<https://www.uptodate.com/contents/laboratory-evaluation-of-the-immune-system>

Buttgereit, F., Burmester, G. R., & Brand, M. D. (2000). Bioenergetics of immune functions: fundamental and therapeutic aspects. *Immunol Today*, *21*(4), 192-199.  
[http://dx.doi.org/10.1016/S0167-5699\(00\)01593-0](http://dx.doi.org/10.1016/S0167-5699(00)01593-0)

Chiereghin, A., Petrisli, E., Ravaioli, M., Morelli, M. C., Turello, G., Squarzone, D., Piccirilli, G., Ambretti, S., Gabrielli, L., Pinna, A. D., Landini, M. P., & Lazzarotto, T. (2017). Infectious agents after liver transplant: etiology, timeline and patients' cell-mediated immunity responses. *Med Microbiol Immunol*, *206*(1), 63-71.  
<https://doi.org/10.1007/s00430-016-0485-7>

Clark, N., & Cotler, S. (2020). *Infectious complications in liver transplantation - UptoDate*. <https://www.uptodate.com/contents/infectious-complications-in-liver-transplantation>

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. <https://doi.org/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. <https://doi.org/10.1111/j.1600-6143.2005.01207.x>  
Intellicyt. (2021). Immune Cell Function Assays.  
<https://intellicyt.com/applications/immune-cell-function/>

Intellicyt. (2023). Immune Cell Function Assays.  
<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.  
<https://doi.org/10.1016/j.trim.2015.09.001>

Kobashigawa, J., Colvin, M., Potena, L., Dragun, D., Crespo-Leiro, M. G., Delgado, J. F., Olymbios, M., Parameshwar, J., Patel, J., Reed, E., Reinsmoen, N., Rodriguez, E. R., Ross, H., Starling, R. C., Tyan, D., Urschel, S., & Zuckermann, A. (2018). The management of antibodies in heart transplantation: An ISHLT consensus document. *J Heart Lung Transplant*, 37(5), 537-547.  
<https://doi.org/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.  
<https://doi.org/10.1097/tp.0000000000002191>

Kowalski, R. J., Post, D. R., Mannon, R. B., Sebastian, A., Wright, H. I., Sigle, G., Burdick, J., Elmagd, K. A., Zeevi, A., Lopez-Cepero, M., Daller, J. A., Gritsch, H. A., Reed, E. F., Jonsson, J., Hawkins, D., & Britz, J. A. (2006). Assessing relative risks of infection and rejection: a meta-analysis using an immune function assay. *Transplantation*, 82(5), 663-668. <https://doi.org/10.1097/01.tp.0000234837.02126.70>

Levine, D. J., Glanville, A. R., Aboyou, C., Belperio, J., Benden, C., Berry, G. J., Hachem, R., Hayes, D., Jr., Neil, D., Reinsmoen, N. L., Snyder, L. D., Sweet, S., Tyan, D., Verleden, G., Westall, G., Yusef, R. D., Zamora, M., & 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.  
<https://doi.org/10.1016/j.healun.2016.01.1223>

Ling, X., Xiong, J., Liang, W., Schroder, P. M., Wu, L., Ju, W., Kong, Y., Shang, Y., Guo, Z., & He, X. (2012). Can immune cell function assay identify patients at risk of infection or rejection? A meta-analysis. *Transplantation*, *93*(7), 737-743.  
<https://doi.org/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.  
<https://doi.org/10.3892/etm.2019.8003>

Maidman, S. D., Gidea, C., Reyentovich, A., Rao, S., Saraon, T., Kadosh, B. S., Narula, N., Carillo, J., Smith, D., Moazami, N., Katz, S., & Goldberg, R. I. (2022). Pre-transplant immune cell function assay as a predictor of early cardiac allograft rejection. *Clin Transplant*, *36*(7), e14745. <https://doi.org/10.1111/ctr.14745>

Monforte, V., Ussetti, P., Castejón, R., Sintes, H., Pérez, V. L., Laporta, R., Sole, A., Cifrián, J. M., Marcos, P. J., Redel, J., Arcos, I. L., Berastegui, C., Alonso, R., Rosado, S., Escriva, J., Iturbe, D., Ovalle, J. P., Vaquero, J. M., López-Meseguer, M., . . . 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*. <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. <https://doi.org/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.  
<https://doi.org/10.1016/j.jaci.2009.08.043>

Picard, C., Al-Herz, W., Bousfiha, A., Casanova, J. L., Chatila, T., Conley, M. E., Cunningham-Rundles, C., Etzioni, A., Holland, S. M., Klein, C., Nonoyama, S., Ochs, H. D., Oksenhendler, E., Puck, J. M., Sullivan, K. E., Tang, M. L., Franco, J. L., & 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. <https://doi.org/10.1007/s10875-015-0201-1>

Piloni, D., Magni, S., Oggionni, T., Benazzo, A., Stella, G., Scudeller, L., Morosini, M., Cova, E., & Meloni, F. (2016). Clinical utility of CD4+ function assessment (ViraCor-IBT ImmuKnow test) in lung recipients. *Transpl Immunol*, *37*, 35-39.  
<https://doi.org/10.1016/j.trim.2016.04.001>

Ravaioli, M., Neri, F., Lazzarotto, T., Bertuzzo, V. R., Di Gioia, P., Stacchini, G., Morelli, M. C., Ercolani, G., Cescon, M., Chiereghin, A., Del Gaudio, M., Cucchetti, A., & Pinna,

A. D. (2015). Immunosuppression Modifications Based on an Immune Response Assay: Results of a Randomized, Controlled Trial. *Transplantation*, 99(8), 1625-1632. <https://doi.org/10.1097/tp.0000000000000650>

Rodrigo, E., Lopez-Hoyos, M., Corral, M., Fabrega, E., Fernandez-Fresnedo, G., San Segundo, D., Pinera, C., & 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. <https://doi.org/10.1002/lt.23497>

Sindhi, R., Ashokkumar, C., Higgs, B. W., Levy, S., Soltys, K., Bond, G., Mazariegos, G., Ranganathan, S., & Zeevi, A. (2016). Profile of the Pleximmune blood test for transplant rejection risk prediction. *Expert Rev Mol Diagn*, 16(4), 387-393. <https://doi.org/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. <http://dx.doi.org/>

Vella, J. (2022, August 12). Transplantation immunobiology -. <https://www.uptodate.com/contents/transplantation-immunobiology>

Velleca, A., Shullo, M. A., Dhital, K., Azeka, E., Colvin, M., DePasquale, E., Farrero, M., García-Guereta, L., Jamero, G., Khush, K., Lavee, J., Pouch, S., Patel, J., Michaud, C. J., Shullo, M., Schubert, S., Angelini, A., Carlos, L., Mirabet, S., . . . Reinhardt, Z. (2022). The International Society for Heart and Lung Transplantation (ISHLT) Guidelines for the Care of Heart Transplant Recipients. *The Journal of Heart and Lung Transplantation*, 0(0). <https://doi.org/10.1016/j.healun.2022.09.023>

Wang, Z., Liu, X., Lu, P., Han, Z., Tao, J., Wang, J., Liu, K., Wu, B., Yin, C., Tan, R., & 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. <https://doi.org/10.1016/j.transproceed.2014.09.109>

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. <https://doi.org/10.1111/ctr.13809>

Xue, F., Gao, W., Qin, T., Wu, C., Luo, Y., Chen, J., Zhou, T., Feng, M., Qiu, B., Zhu, J., He, 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. <https://doi.org/10.21037/tp-20-256>

Zhang, W., Zhong, H., Zhuang, L., Yu, J., Xu, X., Wang, W., Zhang, M., Zhou, L., & 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 Suppl 185), 11-16. <https://doi.org/10.1111/ijcp.12811>

### Policy Update History:

Approval Date	Effective Date; Summary of Changes
09/13/2024	01/01/2025: New policy.