



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 Oklahoma may use reasonable discretion interpreting and applying this policy to services being delivered in a particular case. BCBSOK 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.

Immunohistochemistry

Policy Number: CPCPLAB069

Version 1.0

Approval Date: January 23, 2025

Plan Effective Date: April 15, 2025

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. Code 88342 should be used for the first single antibody procedure and is reimbursed at one unit per specimen, up to four specimens, per date of service.
2. Code 88341 should be used for each additional single antibody per specimen and is reimbursed up to a maximum of 13 units per date of service.
3. Code 88344 should be used for each multiplex antibody per specimen, up to six specimens, per date of service.

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
88341, 88342, 88344

References:

- Fitzgibbons, P. L., Bradley, L. A., Fatheree, L. A., Alsabeh, R., Fulton, R. S., Goldsmith, J. D., Haas, T. S., Karabakhtsian, R. G., Loykasek, P. A., Marolt, M. J., Shen, S. S., Smith, A. T., & Swanson, P. E. (2014). Principles of analytic validation of immunohistochemical assays: Guideline from the College of American Pathologists Pathology and Laboratory Quality Center. *Arch Pathol Lab Med*, 138(11), 1432-1443. <https://doi.org/10.5858/arpa.2013-0610-CP>
- Goldsmith, J. D., Troxell, M. L., Roy-Chowdhuri, S., Colasacco, C. F., Edgerton, M. E., Fitzgibbons, P. L., Fulton, R., Haas, T., Kandalaf, P. L., Kalicanin, T., Lacchetti, C., Loykasek, P., Thomas, N. E., Swanson, P. E., & Bellizzi, A. M. (2024). Principles of Analytic Validation of Immunohistochemical Assays: Guideline Update. *Arch Pathol Lab Med*, 148(6), e111-e153. <https://doi.org/10.5858/arpa.2023-0483-CP>
- Hainsworth, J., & Greco, F. (2023, January 20). *Overview of the classification and management of cancers of unknown primary site*. <https://www.uptodate.com/contents/overview-of-the-classification-and-management-of-cancers-of-unknown-primary-site>
- Hofman, P., Badoual, C., Henderson, F., Berland, L., Hamila, M., Long-Mira, E., Lassalle, S., Roussel, H., Hofman, V., Tartour, E., & Ilie, M. (2019). Multiplexed Immunohistochemistry for Molecular and Immune Profiling in Lung Cancer-Just About Ready for Prime-Time? *Cancers (Basel)*, 11(3). <https://doi.org/10.3390/cancers11030283>
- Kalra, J., & Baker, J. (2017). Multiplex Immunohistochemistry for Mapping the Tumor Microenvironment. *Methods Mol Biol*, 1554, 237-251. https://doi.org/10.1007/978-1-4939-6759-9_17
- Khoury, J. D., Wang, W. L., Prieto, V. G., Medeiros, L. J., Kalhor, N., Hameed, M., Broaddus, R., & Hamilton, S. R. (2018). Validation of Immunohistochemical Assays for Integral Biomarkers in the NCI-MATCH EAY131 Clinical Trial. *Clin Cancer Res*, 24(3), 521-531. <https://doi.org/10.1158/1078-0432.Ccr-17-1597>
- Krämer, A., Bochtler, T., Pauli, C., Baciarello, G., Delorme, S., Hemminki, K., Mileschkin, L., Moch, H., Oien, K., Olivier, T., Patrikidou, A., Wasan, H., Zarkavelis, G., Pentheroudakis, G., & Fizazi, K.

- (2023). Cancer of unknown primary: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. *Ann Oncol*, 34(3), 228-246. <https://doi.org/10.1016/j.annonc.2022.11.013>
- Le Stang, N., Burke, L., Blaizot, G., Gibbs, A. R., Lebailly, P., Clin, B., Girard, N., & Galateau-Salle, F. (2019). Differential Diagnosis of Epithelioid Malignant Mesothelioma With Lung and Breast Pleural Metastasis: A Systematic Review Compared With a Standardized Panel of Antibodies-A New Proposal That May Influence Pathologic Practice. *Arch Pathol Lab Med*. <https://doi.org/10.5858/arpa.2018-0457-OA>
- Lin, F., & Chen, Z. (2014). Standardization of diagnostic immunohistochemistry: literature review and geisinger experience. *Arch Pathol Lab Med*, 138(12), 1564-1577. <https://doi.org/10.5858/arpa.2014-0074-RA>
- Lin, F., & Liu, H. (2014). Immunohistochemistry in undifferentiated neoplasm/tumor of uncertain origin. *Arch Pathol Lab Med*, 138(12), 1583-1610. <https://doi.org/10.5858/arpa.2014-0061-RA>
- Lizotte, P. H., Ivanova, E. V., Awad, M. M., Jones, R. E., Keogh, L., Liu, H., Dries, R., Almonte, C., Herter-Sprie, G. S., Santos, A., Feeney, N. B., Paweletz, C. P., Kulkarni, M. M., Bass, A. J., Rustgi, A. K., Yuan, G. C., Kufe, D. W., Janne, P. A., Hammerman, P. S., . . . Wong, K. K. (2016). Multiparametric profiling of non-small-cell lung cancers reveals distinct immunophenotypes. *JCI Insight*, 1(14), e89014. <https://doi.org/10.1172/jci.insight.89014>
- NCCN. (2023, May 30). *NCCN Clinical Practice Guidelines in Oncology: Genetic/Familial High-Risk Assessment: Colorectal Version 1.2023*. https://www.nccn.org/professionals/physician_gls/pdf/genetics_colon.pdf
- NCCN. (2024, March 23). *NCCN Guidelines Version 4.2024 Invasive Breast Cancer*. National Comprehensive Cancer Network. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf
- Prok, A. L., & Prayson, R. A. (2006). Thyroid transcription factor-1 staining is useful in identifying brain metastases of pulmonary origin. *Annals of Diagnostic Pathology*, 10(2), 67-71. <https://doi.org/10.1016/j.anndiagpath.2005.07.013>
- Shah, A. A., Frierson, H. F., & Cathro, H. P. (2012). Analysis of Immunohistochemical Stain Usage in Different Pathology Practice Settings. <https://doi.org/10.1309/AJCPAGVTCKDXKK0X>
- Tuffaha, M. S. A., Guski, H., & Kristiansen, G. (2018). Immunohistochemistry in Tumor Diagnostics. In M. S. A. Tuffaha, H. Guski, & G. Kristiansen (Eds.), *Immunohistochemistry in Tumor Diagnostics* (pp. 1-9). Springer International Publishing. https://doi.org/10.1007/978-3-319-53577-7_1
- Wolff, A. C., Hammond, M. E., Hicks, D. G., Dowsett, M., McShane, L. M., Allison, K. H., Allred, D. C., Bartlett, J. M., Bilous, M., Fitzgibbons, P., Hanna, W., Jenkins, R. B., Mangu, P. B., Paik, S., Perez, E. A., Press, M. F., Spears, P. A., Vance, G. H., Viale, G., & Hayes, D. F. (2013). Recommendations for human epidermal growth factor receptor 2 testing in breast cancer: American Society of Clinical Oncology/College of American Pathologists clinical practice guideline update. *J Clin Oncol*, 31(31), 3997-4013. <https://doi.org/10.1200/jco.2013.50.9984>
- Wolff, A. C., Hammond, M. E. H., Allison, K. H., Harvey, B. E., Mangu, P. B., Bartlett, J. M. S., Bilous, M., Ellis, I. O., Fitzgibbons, P., Hanna, W., Jenkins, R. B., Press, M. F., Spears, P. A., Vance, G. H., Viale, G., McShane, L. M., & Dowsett, M. (2018). Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. *J Clin Oncol*, 36(20), 2105-2122. <https://doi.org/10.1200/jco.2018.77.8738>
- Wolff, A. C., Somerfield, M. R., Dowsett, M., Hammond, M. E. H., Hayes, D. F., McShane, L. M., Saphner, T. J., Spears, P. A., & Allison, K. H. (2023). Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: ASCO–College of American Pathologists Guideline Update. *Journal of Clinical Oncology*, 41(22), 3867-3872. <https://doi.org/10.1200/JCO.22.02864>

Yamamoto, H., Nozaki, Y., Kohashi, K., Kinoshita, I., & Oda, Y. (2019). Diagnostic utility of pan-Trk immunohistochemistry for inflammatory myofibroblastic tumors. *Histopathology*. <https://doi.org/10.1111/his.14010>

Yamauchi, H., & Bleiweiss, I. (2023, August 25). *HER2 and predicting response to therapy in breast cancer*. <https://www.uptodate.com/contents/her2-and-predicting-response-to-therapy-in-breast-cancer>

Policy Update History:

Approval Date	Effective Date; Summary of Changes
01/23/2025	04/15/2025; Document updated with literature review. Reimbursement Information unchanged. References revised.
03/15/2024	Document updated with literature review. Reimbursement information unchanged. References revised; some added; others removed.
06/15/2023	Document updated with literature review. Reimbursement information unchanged. References revised; some added, others removed.
11/01/2022	New policy