



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.

Flow Cytometry

Policy Number: CPCPLAB001

Version 1.0

Approval Date: October 30, 2024

Plan Effective Date: January 15, 2025

Description

BCBSOK 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. Flow cytometry immunophenotyping of cell surface markers **may be reimbursable** for any of the following conditions:
 - a. For individuals with cytopenias, lymphomas, leukemia, myeloproliferative and lymphoproliferative disorders, or myelodysplastic syndrome;
 - b. For B-cell monitoring for immunosuppressive disorders;
 - c. For T-cell monitoring for HIV infection and AIDS;
 - d. For individuals with mast cell neoplasms;
 - e. For individuals with paroxysmal nocturnal hemoglobinuria;
 - f. For pre-operative or post-operative monitoring of individuals who will undergo or who have undergone organ transplantation;
 - g. For individuals with plasma cell disorders;
 - h. For individuals with primary Immunodeficiencies (PIDs), and PIDs involving T, NK;
 - i. For individuals with primary platelet disorders, (non-neoplastic);
 - j. For individuals with red cell and white cell disorders, (non-neoplastic).
2. Flow cytometry immunophenotyping of cell surface markers **is not reimbursable** for any clinical condition not listed above.

The following reimbursement limitations will apply for flow cytometry:

- a. For flow cytometric immunophenotyping for the assessment of potential hematolymphoid neoplasia, use codes 88184-88189.
 - b. Code 88184 should be used for the first marker, per specimen, and is reimbursable up to a maximum of two units per date of service.
 - c. Code 88185 should be used for each additional marker and is reimbursable up to a maximum of 35 units, per date of service.
 - d. In patients with a neoplasm with an established immunophenotype, subsequent tests for that neoplasm should be limited to diagnostically relevant markers.
 - e. Codes 88187, 88188, and 88189 should not be used together for a single specimen in any combination.
 - f. Codes 88187, 88188, and 88189 are reimbursed at one unit per specimen, up to two specimens, per date of service.
 - g. Codes 88187, 88188, 88189 should not be used in conjunction with codes 86355, 86356, 86357, 86359, 86360, 86361, 86367.
 - h. Use codes 86355, 86357, 86359, 86360, 86361, or 86367 for cell enumeration. These codes are reimbursable as single units only.
3. Measurement of flow-cytometry-deprived DNA content (DNA Index) or cell proliferative activity (S-phase fraction or % S-phase) for prognostic or therapeutic purposes in the routine clinical management of cancers **is not reimbursable**.

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
86355, 86356, 86357, 86359, 86360, 86361, 86367, 88182, 88184, 88185, 88187, 88188, 88189

References

- Abraham, R. S., & Aubert, G. (2016). Flow Cytometry, a Versatile Tool for Diagnosis and Monitoring of Primary Immunodeficiencies. *Clin Vaccine Immunol*, 23(4), 254-271. <https://doi.org/10.1128/cvi.00001-16>
- ACS. (2021). Breast Cancer Ploidy and Cell Proliferation. <https://www.cancer.org/cancer/breast-cancer/understanding-a-breast-cancer-diagnosis/ploidy-and-cell-proliferation.html>
- Adan, A., Alizada, G., Kiraz, Y., Baran, Y., & Nalbant, A. (2017). Flow cytometry: basic principles and applications. *Crit Rev Biotechnol*, 37(2), 163-176. <https://doi.org/10.3109/07388551.2015.1128876>
- Bagwell, C. B., Clark, G. M., Spyrtos, F., Chassevent, A., Bendahl, P. O., Stal, O., Killander, D., Jourdan, M. L., Romain, S., Hunsberger, B., & Baldetorp, B. (2001). Optimizing flow cytometric DNA ploidy and S-phase fraction as independent prognostic markers for node-negative breast cancer specimens. *Cytometry*, 46(3), 121-135. <https://pubmed.ncbi.nlm.nih.gov/11449403/>
- Brown, M., & Wittwer, C. (2000). Flow cytometry: principles and clinical applications in hematology. *Clin Chem*, 46(8 Pt 2), 1221-1229. <https://pubmed.ncbi.nlm.nih.gov/10926916/>
- Carloni, S., Gallerani, G., Tesei, A., Scarpi, E., Verdecchia, G. M., Virzi, S., Fabbri, F., & Arienti, C. (2017). DNA ploidy and S-phase fraction analysis in peritoneal carcinomatosis from ovarian cancer: correlation with clinical pathological factors and response to chemotherapy. *Oncotargets Ther*, 10, 4657-4664. <https://doi.org/10.2147/ott.s141117>
- Cho, K. R., Cooper, K., Croce, S., Djordjevic, B., Herrington, S., Howitt, B., Hui, P., Ip, P., Koebel, M., Lax, S., Quade, B. J., Shaw, P., Vidal, A., Yemelyanova, A., Clarke, B., Hedrick Ellenson, L., Longacre, T. A., Shih, I. M., McCluggage, W. G., . . . Matias-Guiu, X. (2019). International Society of Gynecological Pathologists (ISGyP) Endometrial Cancer Project: Guidelines From the Special Techniques and Ancillary Studies Group. *Int J Gynecol Pathol*, 38 Suppl 1(Iss 1 Suppl 1), S114-s122. <https://doi.org/10.1097/pgp.0000000000000496>
- Christensen, K., Hulick, Peter. (2024). Basic genetics concepts: Chromosomes and cell division. <https://www.uptodate.com/contents/basic-genetics-concepts-chromosomes-and-cell-division>
- Cosma, A., Nolan, G., & Gaudilliere, B. (2017). Mass cytometry: The time to settle down. *Cytometry A*, 91(1), 12-13. <https://doi.org/10.1002/cyto.a.23032>
- D. Arber, M. B., Melissa Cessna, Joan Etzell, Kathryn Foucar, Robert Hasserjian, J. Douglas Rizzo, Karl Theil, Sa Wang, Anthony Smith, R. Bryan Rumble, Nicole Thomas, James Vardiman. (2017). Initial Diagnostic Workup of Acute Leukemia; Guideline From the College of American Pathologists and the American Society of Hematology. *Arch Pathol Lab Med*, 141, 1342-1393. <https://doi.org/10.5858/arpa.2016-0504-CP>
- Davis, B. H., Holden, J. T., Bene, M. C., Borowitz, M. J., Braylan, R. C., Cornfield, D., Gorczyca, W., Lee, R., Maiese, R., Orfao, A., Wells, D., Wood, B. L., & Stetler-Stevenson, M. (2007). 2006 Bethesda International Consensus recommendations on the flow cytometric immunophenotypic analysis of hematolymphoid neoplasia: medical indications. *Cytometry B Clin Cytom*, 72 Suppl 1, S5-13. <https://doi.org/10.1002/cyto.b.20365>

- Ermiah, E., Buhmeida, A., Abdalla, F., Khaled, B. R., Salem, N., Pyrhönen, S., & Collan, Y. (2012). Prognostic value of proliferation markers: immunohistochemical ki-67 expression and cytometric s-phase fraction of women with breast cancer in libya. *J Cancer*, 3, 421-431. <https://doi.org/10.7150/jca.4944>
- Finak, G., Langweiler, M., Jaimes, M., Malek, M., Taghiyar, J., Korin, Y., Raddassi, K., Devine, L., Obermoser, G., Pekalski, M. L., Pontikos, N., Diaz, A., Heck, S., Villanova, F., Terrazzini, N., Kern, F., Qian, Y., Stanton, R., Wang, K., . . . McCoy, J. P. (2016). Standardizing Flow Cytometry Immunophenotyping Analysis from the Human ImmunoPhenotyping Consortium. *Sci Rep*, 6, 20686. <https://doi.org/10.1038/srep20686>
- Frelinger, A. L., 3rd, Rivera, J., Connor, D. E., Freson, K., Greinacher, A., Harrison, P., Kunishima, S., Lordkipanidzé, M., Michelson, A. D., Ramström, S., & Gresele, P. (2021). Consensus recommendations on flow cytometry for the assessment of inherited and acquired disorders of platelet number and function: Communication from the ISTH SSC Subcommittee on Platelet Physiology. *J Thromb Haemost*, 19(12), 3193-3202. <https://doi.org/10.1111/jth.15526>
- Fromm, J. R., Thomas, A., & Wood, B. L. (2009). Flow cytometry can diagnose classical hodgkin lymphoma in lymph nodes with high sensitivity and specificity. *Am J Clin Pathol*, 131(3), 322-332. <https://doi.org/10.1309/ajcpw3un9dyldspb>
- Gawrychowski, J., Lackowska, B., & Gabriel, A. (2003). Prognosis of the surgical treatment of patients with non-small cell lung cancer (NSCLC)--relation to DNA ploidy. *Eur J Cardiothorac Surg*, 23(6), 870-877; discussion 877. <https://pubmed.ncbi.nlm.nih.gov/12829060/>
- Halder, M., Nath, S., & Jha, S. (2017). Flow Cytometry and Its Utility. *Chromosome Structure and Aberrations*, 109-126. https://link.springer.com/chapter/10.1007/978-81-322-3673-3_5
- Harris, L., Fritsche, H., Mennel, R., Norton, L., Ravdin, P., Taube, S., Somerfield, M. R., Hayes, D. F., & Bast, R. C., Jr. (2007). American Society of Clinical Oncology 2007 update of recommendations for the use of tumor markers in breast cancer. *J Clin Oncol*, 25(33), 5287-5312. <https://doi.org/10.1200/jco.2007.14.2364>
- Horowitz, N. S., Eskander, R. N., Adelman, M. R., & Burke, W. (2021). Epidemiology, diagnosis, and treatment of gestational trophoblastic disease: A Society of Gynecologic Oncology evidenced-based review and recommendation. *Gynecologic Oncology*, 163(3), 605-613. <https://doi.org/10.1016/j.ygyno.2021.10.003>
- Jin, J., Mao, X., & Zhang, D. (2024). A differential diagnosis method for systemic CAEBV and the prospect of EBV-related immune cell markers via flow cytometry. *Ann Med*, 56(1), 2329136. <https://doi.org/10.1080/07853890.2024.2329136>
- Johnson, D. B., Dahlman, K. H., Knol, J., Gilbert, J., Puzanov, I., Means-Powell, J., Balko, J. M., Lovly, C. M., Murphy, B. A., Goff, L. W., Abramson, V. G., Crispens, M. A., Mayer, I. A., Berlin, J. D., Horn, L., Keedy, V. L., Reddy, N. M., Arteaga, C. L., Sosman, J. A., & Pao, W. (2014). Enabling a Genetically Informed Approach to Cancer Medicine: A Retrospective Evaluation of the Impact of Comprehensive Tumor Profiling Using a Targeted Next-Generation Sequencing Panel. *Oncologist*, 19(6), 616-622. <https://doi.org/10.1634/theoncologist.2014-0011>
- Kenney, B., Zieske, A., Rinder, H., & Smith, B. (2008). DNA ploidy analysis as an adjunct for the

detection of relapse in B-lineage acute lymphoblastic leukemia. *Leuk Lymphoma*, 49(1), 42-48. <https://doi.org/10.1080/10428190701760052>

Locker, G. Y., Hamilton, S., Harris, J., Jessup, J. M., Kemeny, N., Macdonald, J. S., Somerfield, M. R., Hayes, D. F., & Bast, R. C., Jr. (2006). ASCO 2006 update of recommendations for the use of tumor markers in gastrointestinal cancer. *J Clin Oncol*, 24(33), 5313-5327. <https://doi.org/10.1200/jco.2006.08.2644>

Maguire, O., Tario, J. D., Jr., Shanahan, T. C., Wallace, P. K., & Minderman, H. (2014). Flow cytometry and solid organ transplantation: a perfect match. *Immunol Invest*, 43(8), 756-774. <https://doi.org/10.3109/08820139.2014.910022>

Mangili, G., Montoli, S., De Marzi, P., Sassi, I., Aletti, G., & Taccagni, G. (2008). The role of DNA ploidy in postoperative management of stage I endometrial cancer. *Ann Oncol*, 19(7), 1278-1283. <https://doi.org/10.1093/annonc/mdn041>

McKinnon, K. M. (2018). Flow Cytometry: An Overview. *Curr Protoc Immunol*, 120, 5.1.1-5.1.11. <https://doi.org/10.1002/cpim.40>

NCCN. (2024). *NCCN Clinical Practice Guidelines in Oncology* https://www.nccn.org/professionals/physician_gls/default.aspx

Novikov, N. D., Griffin, G. K., Dudley, G., Drew, M., Rojas-Rudilla, V., Lindeman, N. I., & Dorfman, D. M. (2019). Utility of a Simple and Robust Flow Cytometry Assay for Rapid Clonality Testing in Mature Peripheral T-Cell Lymphomas. *Am J Clin Pathol*, 151(5), 494-503. <https://doi.org/10.1093/ajcp/aqy173>

Paiva, B., Merino, J., & San Miguel, J. F. (2016). Utility of flow cytometry studies in the management of patients with multiple myeloma. *Curr Opin Oncol*, 28(6), 511-517. <https://doi.org/10.1097/cco.0000000000000331>

Panwar, S., Handa, U., Kaur, M., Mohan, H., & Attri, A. K. (2021). Evaluation of DNA ploidy and S-phase fraction in fine needle aspirates from breast carcinoma. *Diagn Cytopathol*, 49(6), 761-767. <https://doi.org/10.1002/dc.24738>

Pinto, A. E., André, S., & Soares, J. (1999). Short-term significance of DNA ploidy and cell proliferation in breast carcinoma: a multivariate analysis of prognostic markers in a series of 308 patients. *Journal of Clinical Pathology*, 52(8), 604. <https://doi.org/10.1136/jcp.52.8.604>

Pinto, A. E., Pires, A., Silva, G., Bicho, C., Andre, S., & Soares, J. (2011). Ploidy and S-phase fraction as predictive markers of response to radiotherapy in cervical cancer. *Pathol Res Pract*, 207(10), 623-627. <https://doi.org/10.1016/j.prp.2011.07.007>

Porwit, A., van de Loosdrecht, A. A., Bettelheim, P., Brodersen, L. E., Burbury, K., Cremers, E., Della Porta, M. G., Ireland, R., Johansson, U., Matarraz, S., Ogata, K., Orfao, A., Preijers, F., Psarra, K., Subira, D., Valent, P., van der Velden, V. H., Wells, D., Westers, T. M., . . . Bene, M. C. (2014). Revisiting guidelines for integration of flow cytometry results in the WHO classification of myelodysplastic syndromes-proposal from the International/European LeukemiaNet Working Group for Flow Cytometry in MDS. *Leukemia*, 28(9), 1793-1798. <https://doi.org/10.1038/leu.2014.191>

Rawstron, A. C., Kreuzer, K. A., Soosapilla, A., Spacek, M., Stehlikova, O., Gambell, P., McIver-

Brown, N., Villamor, N., Psarra, K., Arroz, M., Milani, R., de la Serna, J., Cedena, M. T., Jaksic, O., Nomdedeu, J., Moreno, C., Rigolin, G. M., Cuneo, A., Johansen, P., . . . Montserrat, E. (2018). Reproducible diagnosis of chronic lymphocytic leukemia by flow cytometry: An European Research Initiative on CLL (ERIC) & European Society for Clinical Cell Analysis (ESCCA) Harmonisation project. *Cytometry B Clin Cytom*, *94*(1), 121-128. <https://doi.org/10.1002/cyto.b.21595>

Robinson, J. P., & Roederer, M. (2015). HISTORY OF SCIENCE. Flow cytometry strikes gold. *Science*, *350*(6262), 739-740. <https://doi.org/10.1126/science.aad6770>

Ross, J. S. (1996). DNA ploidy and cell cycle analysis in cancer diagnosis and prognosis. *Oncology (Williston Park)*, *10*(6), 867-882, 887; discussion 887-890. <https://www.cancernetwork.com/view/dna-ploidy-and-cell-cycle-analysis-cancer-diagnosis-and-prognosis>

Seckl, M. J., Sebire, N. J., Fisher, R. A., Golfier, F., Massuger, L., & Sessa, C. (2013). Gestational trophoblastic disease: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology*, *24*, vi39-vi50. <https://doi.org/10.1093/annonc/mdt345>

Svanvik, T., Stromberg, U., Holmberg, E., Marcickiewicz, J., & Sundfeldt, K. (2019). DNA ploidy status, S-phase fraction, and p53 are not independent prognostic factors for survival in endometrioid endometrial carcinoma FIGO stage I-III. *Int J Gynecol Cancer*. <https://doi.org/10.1136/ijgc-2018-000082>

Taniguchi, K., Suzuki, A., Serizawa, A., Kotake, S., Ito, S., Suzuki, K., Yamada, T., Noguchi, T., Amano, K., Ota, M., Muragaki, Y., & Yamamoto, M. (2021). Rapid Flow Cytometry of Gastrointestinal Stromal Tumours Closely Matches the Modified Fletcher Classification. *Anticancer Res*, *41*(1), 131-136. <https://doi.org/10.21873/anticancer.14758>

Thomas, G., Tr, S., George, S. P., Somanathan, T., Sarojam, S., Krishnankutti, N., Sreedharan, H., & Ankathil, R. (2020). Prognostic Implications of DNA Repair, Ploidy and Telomerase in the Malignant Transformation Risk Assessment of Leukoplakia. *Asian Pac J Cancer Prev*, *21*(2), 309-316. <https://doi.org/10.31557/apjcp.2020.21.2.309>

UIHC. (2016). Cancer diagnostic tests and blood tests word list. <https://uihc.org/health-topics/cancer-diagnostic-tests-and-blood-tests-word-list>

Van der Aa, N., Cheng, J., Mateiu, L., Zamani Esteki, M., Kumar, P., Dimitriadou, E., Vanneste, E., Moreau, Y., Vermeesch, J. R., & Voet, T. (2013). Genome-wide copy number profiling of single cells in S-phase reveals DNA-replication domains. *Nucleic Acids Res*, *41*(6), e66. <https://doi.org/10.1093/nar/gks1352>

Verbsky, J., & Routes, J. (2023, October 26, 2023). *Flow cytometry for the diagnosis of primary immunodeficiencies*. <https://www.uptodate.com/contents/flow-cytometry-for-the-diagnosis-of-primary-immunodeficiencies>

Wang, Z., Guo, M., Zhang, Y., Xu, S., Cheng, H., Wu, J., Zhang, W., Hu, X., Yang, J., Wang, J., & Tang, G. (2019). The applicability of multiparameter flow cytometry for the detection of minimal residual disease using different-from-normal panels to predict relapse in patients with acute myeloid leukemia after allogeneic transplantation. *Int J Lab Hematol*, *41*(5), 607-614. <https://doi.org/10.1111/ijlh.13070>

Policy Update History

Approval Date	Effective Date; Summary of Changes
10/30/2024	01/15/2025: Document updated with literature review. The following changes were made to Reimbursement Information: Statement 1f revised to include pre-operative and now reads: For preoperative or post-operative monitoring of individuals who will undergo or who have undergone organ transplantation. Removed the Bill Type Codes. References revised; some added, others updated.
11/01/2023	11/01/2023: Document updated with literature review. Reimbursement information revised for clarity. References revised; some added; others removed. Measurement of flow-cytometry-deprived DNA (DNA Index) or cell proliferative activity (S-phase fraction or % S-phase) for prognostic or therapeutic purposes in the routine clinical management of cancers is not reimbursable was previously addressed on CPCPLAB066 DNA Ploidy Cell Cycle Analysis.
11/1/2022	11/1/2022: New policy