

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.

In Vitro Chemoresistance and Chemosensitivity Assays

Policy Number: CPCPLAB030

Version 1.0

Approval Date: Nov. 19, 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. In vitro chemosensitivity assays, (e.g., histoculture drug response assay, fluorescent cytoprint assay) **are not reimbursable.**
2. In vitro chemoresistance assays, (e.g., extreme drug resistance [EDR] assays) **are 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
81535, 81536, 86849, 88104, 88199, 88305, 88313, 88358, 89050, 89240, 0564T, 0083U, 0248U, 0249U, 0285U, 0525U

References:

Brower, S. L., Fensterer, J. E., & Bush, J. E. (2008). The ChemoFx® Assay: An Ex Vivo Chemosensitivity and Resistance Assay for Predicting Patient Response to Cancer Chemotherapy. In G. Mor & A. B. Alvero (Eds.), *Apoptosis and Cancer: Methods and Protocols* (pp. 57-78). Humana Press. https://doi.org/10.1007/978-1-59745-339-4_6

Burstein, H. J., Mangu, P. B., Somerfield, M. R., Schrag, D., Samson, D., Holt, L., Zelman, D., & Ajani, J. A. (2011). American Society of Clinical Oncology clinical practice guideline update on the use of chemotherapy sensitivity and resistance assays. *J Clin Oncol*, 29(24), 3328-3330. <https://doi.org/10.1200/jco.2011.36.0354>

Chen, Z., Zhang, S., Ma, S., Li, C., Xu, C., Shen, Y., Zhao, J., & Miao, L. (2018). Evaluation of the in vitro Chemosensitivity and Correlation with Clinical Outcomes in Lung Cancer using the ATP-TCA. *Anticancer Agents Med Chem*, 18(1), 139-145. <https://doi.org/10.2174/1871520617666170419123713>

Grendys, E. C., Jr., Fiorica, J. V., Orr, J. W., Jr., Holloway, R., Wang, D., Tian, C., Chan, J. K., & Herzog, T. J. (2014). Overview of a chemoresponse assay in ovarian cancer. *Clin Transl Oncol*, 16(9), 761-769. <https://doi.org/10.1007/s12094-014-1192-8>

Hatok, J., Babusikova, E., Matakova, T., Mistuna, D., Dobrota, D., & Racay, P. (2009). In vitro assays for the evaluation of drug resistance in tumor cells. *Clin Exp Med*, 9(1), 1-7. <https://doi.org/10.1007/s10238-008-0011-3>

Hoffman, R. M. (2018). Clinical Correlation of the Histoculture Drug Response Assay in Gastrointestinal Cancer. *Methods Mol Biol*, 1760, 61-72. https://doi.org/10.1007/978-1-4939-7745-1_7

Howard, C. M., Valluri, J., Alberico, A., Julien, T., Mazagri, R., Marsh, R., Alastair, H., Cortese, A., Griswold, M., Wang, W., Denning, K., Brown, L., & Claudio, P. P. (2017). Analysis of Chemopredictive Assay for Targeting Cancer Stem Cells in Glioblastoma Patients. *Transl Oncol*, 10(2), 241-254. <https://doi.org/10.1016/j.tranon.2017.01.008>

Karam, A. K., Chiang, J. W., Fung, E., Nossov, V., & Karlan, B. Y. (2009). Extreme drug resistance assay results do not influence survival in women with epithelial ovarian cancer. *Gynecol Oncol*, 114(2), 246-252. <https://doi.org/https://doi.org/10.1016/j.ygyno.2009.02.022>

KIYATEC. (2023). Who We Are. <https://www.kiyatec.com/about#:~:text=Our%20ex%20vivo%203D%20cell%20culture%20platforms%20enable,vivo%20efficacy%29%20to%20investigational%20and%20FDA-cleared%20cancer%20therapies>

Krivak, T. C., Lele, S., Richard, S., Secord, A. A., Leath, C. A., 3rd, Brower, S. L., Tian, C., & Moore, R. G. (2014). A chemoresponse assay for prediction of platinum resistance in primary ovarian cancer. *Am J Obstet Gynecol*, 211(1), 68.e61-68. <https://doi.org/10.1016/j.ajog.2014.02.009>

Kwon, H. Y., Kim, I. K., Kang, J., Sohn, S. K., & Lee, K. Y. (2016). In Vitro Adenosine Triphosphate-Based Chemotherapy Response Assay as a Predictor of Clinical Response to Fluorouracil-Based Adjuvant Chemotherapy in Stage II Colorectal Cancer. *Cancer Res Treat*, 48(3), 970-977. <https://doi.org/10.4143/crt.2015.140>

NCCN. (2023a). *NCCN Clinical Practice Guidelines in Oncology*. https://www.nccn.org/professionals/physician_gls/default.aspx

NCCN. (2023b). *NCCN Clinical Practice Guidelines in Oncology; Ovarian Cancer v 1.2021* https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf

Pierian. (2023). Products: ChemoINTEL™. <https://pierianbio.com/project/chemo-intel/>

RGCC. (2023). *Onconomics RGCC*. <https://www.rgcc-group.com/tests/onconomics-plus-rgcc/>

Rutherford, T., Orr, J., Jr., Grendys, E., Jr., Edwards, R., Krivak, T. C., Holloway, R., Moore, R. G., Puls, L., Tillmanns, T., Schink, J. C., Brower, S. L., Tian, C., & Herzog, T. J. (2013). A prospective study evaluating the clinical relevance of a chemoresponse assay for treatment of patients with persistent or recurrent ovarian cancer. *Gynecol Oncol*, 131(2), 362-367. <https://doi.org/10.1016/j.ygyno.2013.08.009>

Schrag, D., Garewal, H. S., Burstein, H. J., Samson, D. J., Von Hoff, D. D., & Somerfield, M. R. (2004). American Society of Clinical Oncology Technology Assessment: chemotherapy sensitivity and resistance assays. *J Clin Oncol*, 22(17), 3631-3638. <https://doi.org/10.1200/jco.2004.05.065>

Shuford, S., Lipinski, L., Abad, A., Smith, A. M., Rayner, M., O'Donnell, L., Stuart, J., Mechtler, L. L., Fabiano, A. J., Edenfield, J., Kanos, C., Gardner, S., Hodge, P., Lynn, M., Butowski, N. A., Han, S. J., Redjal, N., Crosswell, H. E., Vibat, C. R. T., . . . DesRochers, T. M. (2021). Prospective prediction of clinical drug response in high-grade gliomas using an ex vivo 3D cell culture assay. *Neurooncol Adv*, 3(1), vdab065. <https://doi.org/10.1093/noajnl/vdab065>

Strickland, S. A., Raptis, A., Hallquist, A., Rutledge, J., Chernick, M., Perree, M., Talbott, M. S., & Presant, C. A. (2013). Correlation of the microculture-kinetic drug-induced apoptosis assay with patient outcomes in initial treatment of adult acute myelocytic leukemia. *Leuk Lymphoma*, 54(3), 528-534. <https://doi.org/10.3109/10428194.2012.722217>

Tatar, B., Boyraz, G., Selçuk, İ., Doğan, A. K., Usubütün, A., & Tuncer, Z. S. (2016). In vitro chemosensitivity in ovarian carcinoma: Comparison of three leading assays. In *J Turk Ger Gynecol Assoc* (Vol. 17, pp. 35-40). <https://doi.org/10.5152/jtgga.2016.16017>

Theralink. (2023). Theralink: Precision Medicine for Life. <https://theralink.com/theralink#:~:text=The%20Theralink%20assay%20uses%20Reverse%20Phase%20Protein%20Array,for%20most%20FDA-approved%20and%20investigational%20therapies%20for%20cancer>

Policy Update History:

Approval Date	Effective Date; Summary of Changes
11/19/2024	01/01/2025: Added new CPT code 0525U effective 01/01/2025.
09/13/2024	01/01/2025: New policy.