

<b>MEDICAL POLICY</b>	<b>Chemoresistance and Chemosensitivity Assays</b>	
<b>Effective Date: 04/01/2020</b>   <div style="text-align: right;">4/1/2020</div>	Section: LAB	Policy No: 169
	Medical Policy Committee Approval Date: 12/16  Technology Assessment Committee Approved Date: 2/00; 2/01; 3/02; 3/03; 1/08; 10/10; 11/12; 10/14; 11/14; 10/15; 12/16; 2/18; 8/19; 03/2020	
Medical Officer	Date	

**See Policy CPT/HCPCS CODE section below for any prior authorization requirements**

**SCOPE:**

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as “Company” and collectively as “Companies”).

**APPLIES TO:**

All lines of business

**BENEFIT APPLICATION**

Medicaid Members

*Oregon:* Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

**POLICY CRITERIA**

Chemoresistance and chemosensitivity assays are considered **investigational and are not covered** in the treatment of cancer. Examples of non-covered tests include, but are not limited to the following:

- BioSpeciFx®
- ChemoFX®
- CorrectChemo®
- Ex-Vivo Analysis of Programmed Cell Death (EVA-PCD)
- Histoculture Drug Response Assay®
- Oncotech Extreme Drug Resistance [EDR] Assay for Solid Tumor®

Link to [Policy Summary](#)

<b>MEDICAL POLICY</b>	<b>Chemoresistance and Chemosensitivity Assays</b>
-----------------------	--

**CPT CODES**

All Lines of Business	
Not Covered	
81535	Oncology (gynecologic), live tumor cell culture and chemotherapeutic response by DAPI stain and morphology, predictive algorithm reported as a drug response score; first single drug or drug combination
81536	Oncology (gynecologic), live tumor cell culture and chemotherapeutic response by DAPI stain and morphology, predictive algorithm reported as a drug response score; each additional single drug or drug combination (List separately in addition to code for primary procedure)
<b>Unlisted Codes</b> All unlisted codes will be reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is billed related to services addressed in this policy then it will be <b>denied as not covered</b> .	
86849	Tissue Typing Immunological Procedures
87999	Unlisted microbiology procedure
88299	Unlisted cytogenetic study
89240	Unlisted miscellaneous pathology test

**DESCRIPTION**

Protocols for treating cancer are currently based on the type and stage of the cancer. Chemoresistance and chemosensitivity (e.g., Oncotech Assays and Chemo FX Assay) tests have been proposed as a method predicting the effect of specific drugs on tumors in order to assist in chemotherapy selection. However, current evidence has not demonstrated that these tests have been used to alter treatment decisions which have led to improved health outcomes.

**REVIEW OF EVIDENCE**

A review of the ECRI, Hayes, Cochrane, and PubMed databases was conducted regarding the use of chemoresistance and chemosensitivity assays as a method of selecting chemotherapeutic treatment for cancer. Below is a summary of the available evidence identified through February of 2020.

In 2013, Rutherford et al. published a prospective study evaluating the clinical relevance of a chemoresponse assay in the treatment of persistent or recurrent ovarian cancer.<sup>1</sup> A total of 262 patients were treated with one of fifteen treatments prescribed by the oncologist. Chemoresponse assays were performed and classified treatment as sensitive (S), intermediate (I), or resistant (R). Results indicate that patients treated with an assay-sensitive treatment had an improved clinical outcome (mean overall survival was increased by 14 months; 37.5 months for S vs. 23.9 months for I+R, p=0.010); however, this study did not evaluate how assay results were used to alter treatment decisions or improve progression-free or overall survival. Although this and other studies may establish the clinical validity of

chemoresponse assays by demonstrating a correlation of response to test results, current evidence does not show how assay-guided therapy may be used to alter outcomes.

A 2015 literature review by Richard and colleagues on the use of the ChemoFX assay to identify effective treatment for epithelial ovarian cancer suggest that the assay is an effective option for improving patient outcomes.<sup>2</sup> However, authors indicated that the evidence remains limited by the lack of comparison between multiple therapies and other factors such as the possibility of toxicity that were not addressed.

Additional studies have been identified which are limited by a non-randomized design, small sample size and short-term follow-up.<sup>3,4</sup>

## CLINICAL PRACTICE GUIDELINES

### National Comprehensive Cancer Network (NCCN)

The NCCN clinical practice guidelines for ovarian cancer (including fallopian tube cancer and primary peritoneal cancer) (v.3.2019) principles of systemic therapy have a general information bullet that stated:<sup>5</sup>

- Chemosensitivity/resistance and/or other biomarker assays are being used at some NCCN Member Institutions for decisions related to future chemotherapy in situations where there are multiple equivalent chemotherapy options available. The current level of evidence is not sufficient to supplant standard-of-care chemotherapy (category 3).

Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

No other NCCN guidelines were identified that referenced chemosensitivity/chemoresistance assays.

### American Society of Clinical Oncology (ASCO)

The 2011 ASCO clinical practice guideline update on the use of chemotherapy sensitivity and resistance assays recommends that the assays be used only in the clinical trial setting.<sup>6</sup>

## CENTERS FOR MEDICARE & MEDICAID

As of 02/21/2020, the following Centers for Medicare & Medicaid (CMS) coverage guidance was identified which support our investigational denial of chemoresistance and chemosensitivity assays: NCD [190.7](#) and LCD [L36353](#).<sup>7,8</sup>

## POLICY SUMMARY

The current evidence is insufficient to support the use of chemoresistance or chemosensitivity assays for patients with or without cancer. In addition, no evidence-based clinical practice guidelines were identified which support the use of these assays for any population.

## INSTRUCTIONS FOR USE

Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Companies reserve the right to determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days notice of policy changes that are restrictive in nature.

The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement.

## REGULATORY STATUS

### Mental Health Parity Statement

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

## REFERENCES

1. Rutherford T, Orr J, Jr., Grendys E, Jr., et al. A prospective study evaluating the clinical relevance of a chemoresponse assay for treatment of patients with persistent or recurrent ovarian cancer. *Gynecol Oncol*. 2013;131(2):362-367. <https://www.ncbi.nlm.nih.gov/pubmed/23954900>
2. Richard S, Wells A, Connor J, Price F. Use of ChemoFx(R) for Identification of Effective Treatments in Epithelial Ovarian Cancer. *PLoS Curr*. 2015;7. <https://www.ncbi.nlm.nih.gov/pubmed/26213638>
3. Howard CM, Valluri J, Alberico A, et al. Analysis of Chemopredictive Assay for Targeting Cancer Stem Cells in Glioblastoma Patients. *Transl Oncol*. 2017;10(2):241-254. <https://www.ncbi.nlm.nih.gov/pubmed/28199863>
4. Jamal BT, Grillone GA, Jalisi S. Chemoresponse Assay in Head and Neck Cancer Patients: A Three-Year Follow Up. *J Clin Diagn Res*. 2017;11(5):XC01-XC03. <https://www.ncbi.nlm.nih.gov/pubmed/28658890>
5. The National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Ovarian Cancer. Including Fallopian Tube Cancer and Primary Peritoneal Cancer. Version 3.2019 - November 26, 2019. [https://www.nccn.org/professionals/physician\\_gls/pdf/ovarian.pdf](https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf). Accessed 02/20/2020.

<b>MEDICAL POLICY</b>	<b>Chemoresistance and Chemosensitivity Assays</b>
-----------------------	--

6. Burstein HJ, Mangu PB, Somerfield MR, et al. American Society of Clinical Oncology clinical practice guideline update on the use of chemotherapy sensitivity and resistance assays. *J Clin Oncol*. 2011;29(24):3328-3330. <https://www.ncbi.nlm.nih.gov/pubmed/21788567>
7. Centers for Medicaid & Medicare Services. Local Coverage Determination (LCD): Lab: Special Histochemical Stains and Immunohistochemical Stains (L36353). Revision Effective Date: For services performed on or after 12/01/2019. <https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=36353>. Accessed 02/20/2020.
8. Centers for Medicaid & Medicare Services. National Coverage Determination (NCD) for Human Tumor Stem Cell Drug Sensitivity Assays (190.7). Effective Date of this Version: 7/1/1996. <https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=253>. Accessed 02/20/2020.