Medical Policy

PARAMOUNT

HMO AND PPO
ELITE (MEDICARE ADVANTAGE)
MARKETPLACE

In Vitro Chemoresistance & Chemosensitivity Assays

Policy Number: PG0122
Last Review: 09/01/2024

GUIDELINES:

- This policy does not certify benefits or authorization of benefits, which is designated by each individual policyholder terms, conditions, exclusions, and limitations contract. It does not constitute a contract or guarantee regarding coverage or reimbursement/payment. Self-Insured group specific policy will supersede this general policy when group supplementary plan document or individual plan decision directs otherwise.
- Paramount applies coding edits to all medical claims through coding logic software to evaluate the accuracy and adherence to accepted national standards.
- This medical policy is solely for guiding medical necessity and explaining correct procedure reporting used to assist in making coverage decisions and administering benefits.

SCOPE:

X Professional
X Facility

DESCRIPTION:

In order to avoid ineffective chemotherapy toxicity, the intent of chemosensitivity and chemoresistance assays is to assist oncologists with the selection of chemotherapy drugs at initial diagnosis and tumor recurrence. The difference in these assays is determined by the processing method.

- A chemosensitivity assay is a laboratory test performed to evaluate tumor growth and its response to a known chemotherapeutic drug or panel of drugs.
- A chemoresistance assay is a laboratory test used to identify chemotherapeutic agents which may be ineffective against tumor growth. A chemoresistance assay determines “extreme drug resistance” when tumor cell cultures are exposed to high concentrations of selected agent(s) for prolonged exposure times. A chemoresistance assay is used to deselect potentially ineffective therapeutic agents.

Chemotherapy sensitivity and resistance assays may also be called human tumor stem cell drug sensitivity assays, non-clonogenic or clonogenic cytotoxic drug resistance assays, tumor stem cell assays, or differential staining cytotoxic assays. These assays are intended to provide oncologists with information which assists in the selection of chemotherapy drugs, to select potentially more effective chemotherapy regimens, and to avoid the toxicity of potentially ineffective chemotherapy drugs for an individual.

Multiple sensitivity assays, also referred to as in vitro assays, are available. These laboratory tests are performed in a test tube and measure the activity of a drug on a sample of tissue. Though the assays may differ in their technologies and processes in measuring sensitivity, they share four basic steps: isolation of tumor cells, incubation of cells with anticancer drugs, assessment of cell growth or survival, and interpretation of results.

POLICY:

Paramount Commercial Insurance Plans and Elite (Medicare Advantage) Plans

- **In vitro chemoresistance or chemosensitivity assays are non-covered.**

COVERAGE CRITERIA:

Paramount Commercial Insurance Plans and Elite (Medicare Advantage) Plans

Paramount does not cover in vitro chemoresistance or chemosensitivity assays because such testing is

considered experimental/investigational, for all indications. This includes, but may not be limited to, the following:

- Adenosine Triphosphate (ATP)
- 3D Predict Glioma
- Adenosine Triphosphate Bioluminescence
- ChemoFx assay
- Clonogenic Cytotoxic Drug Resistance
- CorrectChemo
- Cytoprint
- Differential staining cytotoxic (DiSC) assay
- Extreme drug resistance (EDR) assay (an in vivo assay designed to predict the sensitivity and resistance of solid tumor cultures to a variety of increasing doses of selected chemotherapy agents.)
- Fluorescence (cytoprint) assay
- Fluorometric Microculture Cytotoxicity
- Histoculture Drug Response Assay (HDRA)
- Human tumor cloning assay (HTCA)
- Methyl thiazolyl-diphenyl-tetrazolium bromide (MTT) assay
- Microculture kinetic (MiCK) assay
- Nonclonogenic Clonogenic Cytotoxic Drug Resistance
- Onco4D™
- Theralink®
- Tritiated Thymine
- Tumor stem cell assay

Evidence from available studies is insufficient to conclude that in vitro chemosensitivity or chemoresistance testing leads to improved health management or outcomes.

CODING/BILLING INFORMATION:

The appearance of a code in this section does not necessarily indicate coverage. Codes that are covered may have selection criteria that must be met. Payment for supplies may be included in payment for other services rendered.

CPT CODES	
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)
81599	Unlisted multianalyte assay with algorithmic analysis [Non-covered when specified as in vitro chemosensitivity or in vitro chemoresistance assay, ex vivo analysis of programmed cell death]
84999	Unlisted chemistry procedure [Non-covered when specified as in vitro chemosensitivity or in vitro chemoresistance assay, ex vivo analysis of programmed cell death]
86849	Unlisted immunology procedure [Non-covered when specified as in vitro chemosensitivity or in vitro chemoresistance assay, ex vivo analysis of programmed cell death]
87999	Unlisted microbiology procedure [Non-covered when specified as in vitro chemosensitivity or in vitro chemoresistance assay]
88104	Cytopathology, fluids, washings or brushings, except cervical or vaginal; smears with interpretation [Non-covered when specified as in vitro chemosensitivity or in vitro chemoresistance assay]
88199	Unlisted cytopathology procedure [Non-covered when specified as in vitro chemosensitivity or in vitro chemoresistance assay]
88305	Level IV - Surgical pathology, gross and microscopic examination [Non-covered when specified as in vitro chemosensitivity or in vitro chemoresistance assay]
88313	Special stain including interpretation and report; Group II, all other (eg, iron, trichrome), except stain for microorganisms, stains for enzyme constituents, or immunocytochemistry and

	immunohistochemistry [Non-covered when specified as in vitro chemosensitivity or in vitro chemoresistance assay]
89050	Cell count, miscellaneous body fluids (eg, cerebrospinal fluid, joint fluid), except blood [Non-covered when specified as in vitro chemosensitivity or in vitro chemoresistance assay]
89240	Unlisted miscellaneous pathology test [Non-covered when specified as in vitro chemosensitivity or in vitro chemoresistance assay]
0083U	Oncology, response to chemotherapy drugs using motility contrast tomography, fresh or frozen tissue, reported as likelihood of sensitivity or resistance to drugs or drug combinations
0248U	Oncology (brain), spheroid cell culture in a 3D microenvironment, 12 drug panel, tumor-response prediction for each drug
0249U	Oncology (breast), semiquantitative analysis of 32 phosphoproteins and protein analytes, includes laser capture microdissection, with algorithmic analysis and interpretative report
0285U	Oncology, response to radiation, cell-free DNA, quantitative branched chain DNA amplification, plasma, reported as a radiation toxicity score
0324U	Oncology (ovarian), spheroid cell culture, 4-drug panel (carboplatin, doxorubicin, gemcitabine, paclitaxel), tumor chemotherapy response prediction for each drug
0325U	Oncology (ovarian), spheroid cell culture, poly (ADP-ribose) polymerase (PARP) inhibitors (niraparib, olaparib, rucaparib, velparib), tumor response prediction for each drug New Code
0564T	Oncology, chemotherapeutic drug cytotoxicity assay of cancer stem cells (CSCs), from cultured CSCs and primary tumor cells, categorical drug response reported based on percent of cytotoxicity observed, a minimum of 14 drugs or drug combinations

REVISION HISTORY EXPLANATION: ORIGINAL EFFECTIVE DATE: 10/01/2012

Date	Explanation & Changes
08/20/2015	• Changed title from ChemoFx® (Assay Precision Therapeutics) to PG0122 In Vitro Chemoresistance and Chemosensitivity Assays (ChemoFx) • Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG)
12/17/2015	• Added effective 1/1/16 new codes 81535 & 81536 • Removed codes 86849, & 89240 • Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG)
07/22/2016	• Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG)
01/25/2018	• Policy reviewed and updated to reflect most current clinical evidence per The Technology Assessment Working Group (TAWG)
12/15/2020	• Medical policy placed on the new Paramount Medical policy format
02/08/2023	• Medical Policy updated to reflect Medicaid coverage to Anthem as of 02/01/2023
10/01/2023	• Medical Policy reviewed and updated to reflect the most current clinical evidence • Added procedure codes unlisted codes 81599, 86849, 87999, 89240 - Non-covered when specified as in vitro chemosensitivity or in vitro chemoresistance assay. Added procedure codes 0083U, 0248U, 0324U, 0325U, 0564T
02/16/2024	• Medical Policy placed on the new Paramount Medical Policy format
09/01/2024	• Medical Policy reviewed and updated to reflect the most current clinical evidence • Added procedures 88104, 88199, 88305, 88313, 89050, 0249U, 0285U

Paramount reserves the right to review and revise our policies periodically when necessary. When there is an update, we will publish the most current policy to
https://www.paramounthealthcare.com/providers/medical-policies/policy-library

REFERENCES/RESOURCES

Centers for Medicare and Medicaid Services, CMS Manual System and other CMS publications and services https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Internet-Only-Manuals-IOMs

American Medical Association, *Current Procedural Terminology (CPT®)* and associated publications and services https://www.ama-assn.org/amaone/cpt-current-procedural-terminology

Centers for Medicare and Medicaid Services, Healthcare Common Procedure Coding System, HCPCS Release and Code Sets https://www.cms.gov/Medicare/Coding/HCPCSReleaseCodeSets/HCPCS-Quarterly-Update

U.S. Preventive Services Task Force, https://www.uspreventiveservicestaskforce.org/uspstf/
Industry Standard Review

Hayes, Inc., https://www.hayesinc.com/

Industry Standard Review

Medical Policy History – Prior to 09/01/2024
DESCRIPTION:
In order to avoid ineffective chemotherapy toxicity, the intent of chemosensitivity and chemoresistance assays is to assist oncologists with the selection of chemotherapy drugs at initial diagnosis and tumor recurrence. The difference in these assays is determined by the processing method.

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POLICY:

Paramount Commercial Insurance Plans and Elite (Medicare Advantage) Plans

- **In vitro chemoresistance or chemosensitivity assays are non-covered.**

COVERAGE CRITERIA:
Paramount Commercial Insurance Plans and Elite (Medicare Advantage) Plans
Paramount does not cover in vitro chemoresistance or chemosensitivity assays because such testing is considered experimental/investigational, for all indications. This includes, but may not be limited to, the following:

- Adenosine Triphosphate (ATP)
- 3D Predict Glioma
- Adenosine Triphosphate Bioluminescence

- ChemoFx assay
- Clonogenic Cytotoxic Drug Resistance
- CorrectChemo
- Cytoprint
- Differential staining cytotoxic (DiSC) assay
- Extreme drug resistance (EDR) assay (an in vivo assay designed to predict the sensitivity and resistance of solid tumor cultures to a variety of increasing doses of selected chemotherapy agents.)
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- Histoculture Drug Response Assay (HDRA)
- Human tumor cloning assay (HTCA)
- Methyl thiazolyl-diphenyl-tetrazolium bromide (MTT) assay
- Microculture kinetic (MiCK) assay
- Nonclonogenic Clonogenic Cytotoxic Drug Resistance
- Onco4D™
- Theralink®
- Tritiated Thymine
- Tumor stem cell assay

Evidence from available studies is insufficient to conclude that in vitro chemosensitivity or chemoresistance testing leads to improved health management or outcomes.

Medical Policy History – Prior to 02/08/2023

DESCRIPTION
A chemosensitivity assay is a laboratory test performed to evaluate tumor growth and its response to a known chemotherapeutic drug or panel of drugs. A chemoresistance assay is a laboratory test used to identify chemotherapeutic agents that may be ineffective against tumor growth. Both techniques have been proposed as an aid in the selection of cancer treatments based on responsiveness of individual tumors.

Multiple sensitivity assays, also referred to as in vitro assays, are available. These laboratory tests are performed in a test tube and measure the activity of a drug on a sample of tissue. Though the assays may differ in their technologies and processes in measuring sensitivity, they share four basic steps: isolation of tumor cells, incubation of cells with anticancer drugs, assessment of cell growth or survival and interpretation of results.

POLICY

Paramount Commercial Plans, Medicare Advantage Plans and Paramount Medicaid Advantage
In vitro chemoresistance or chemosensitivity assays (81535, 81536) are non-covered.

COVERAGE CRITERIA
Paramount Commercial Plans, Medicare Advantage Plans and Paramount Medicaid Advantage
Paramount does not cover in vitro chemoresistance or chemosensitivity assays because such testing is considered experimental, investigational and unproven for all indications. This includes, but may not be limited to, the following:
- ChemoFx assay
- Differential staining cytotoxic (DiSC) assay
- Extreme drug resistance (EDR) assay
- Fluorescence (cytoprint) assay

- Human tumor cloning assay (HTCA)
- Methyl thiazolyl-diphenyl-tetrazolium bromide (MTT) assay
- Microculture kinetic (MiCK) assay
- Tumor stem cell assay

CODING/BILLING INFORMATION

The inclusion or exclusion of a code in this section does not necessarily indicate coverage. Codes referenced in this clinical policy are for informational purposes only.

Codes that are covered may have selection criteria that must be met.

Payment for supplies may be included in payment for other services rendered.

CPT CODES	
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 (New Code Effective 1/1/16)
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) (New Code Effective 1/1/16)
84999	Unlisted chemistry procedure