Medicare Medical Policy

Chemosensitivity and Chemoresistance Assays (CSRAs)

MEDICARE MEDICAL POLICY NUMBER: 329

Effective Date: 1/1/2025

Last Review Date: 12/2024

Next Annual Review: 5/2025

INSTRUCTIONS FOR USE: Company Medicare Medical Policies serve as guidance for the administration of plan benefits and do not constitute medical advice nor a guarantee of coverage. Company Medicare Medical Policies are reviewed annually to guide the coverage or non-coverage decision-making process for services or procedures in accordance with member benefit contracts (otherwise known as Evidence of Coverage or EOCs) and Centers of Medicare and Medicaid Services (CMS) policies, manuals, and other CMS rules and regulations. In the absence of a CMS coverage determination or specific regulation for a requested service, item or procedure, Company policy criteria or applicable utilization management vendor criteria may be applied. These are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. 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. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

The Company reserves the right to determine the application of Medicare Medical Policies and make revisions to these policies at any time. Any conflict or variance between the EOC and Company Medical Policy will be resolved in favor of the EOC.

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

PRODUCT AND BENEFIT APPLICATION

☒ Medicare Only

MEDICARE COVERAGE CRITERIA

IMPORTANT NOTE: More than one Centers for Medicare and Medicaid Services (CMS) reference may apply to the same health care service, such as when more than one coverage policy is available (e.g., both an NCD and LCD exist). All references listed should be considered for coverage decision-making. The Company uses the most current version of a Medicare reference available at the time of publication; however, these websites are not maintained by the Company, so Medicare references and their corresponding hyperlinks may change at any time. If there is a conflict between the Company Medicare Medical Policy and CMS guidance, the CMS guidance will govern.

Service	Medicare Guidelines
*Chemotherapy and Drug **Sensitivity** Assays for **Stem Cell Tumors** (e.g., the Fluorescent Cytoprint Assay, ChemoID [0564T, 0435U])*	National Coverage Determination (NCD): Human Tumor Stem Cell Drug Sensitivity Assays (190.7)
Onco4D™, by Animated Dynamics Inc. (0083U; Indiana)	LCD: Special Histochemical Stains and Immunohistochemical Stains (L36805) *(This LCD reads, "Chemosensitivity profile tumor panels, regardless of whether it is performed by IHC or chromogenic in-situ hybridization (CISH), is not reasonable and necessary for the reasons cited above and is not a Medicare covered service."*
General Chemosensitivity and Chemoresistance Assay (CSRA) Testing *Includes 3D Predict™ tests (KIYATEC® Inc.; South Carolina)* • *3D Predict Glioma test (0248U)* • *3D Predict™ Ovarian Doublet Panel* • *3D Predict™ Ovarian PARP Panel* • *3D Predict™ Ovarian test (0525U)*	• **Testing performed in AK, ID, OR, WA, UT, AZ, MT, ND, SD, or WY:** Local Coverage Determinations (LCD): In Vitro Chemosensitivity & Chemoresistance Assays (L37630) • **Testing performed in CA or NV:** Local Coverage Determinations (LCD): In Vitro Chemosensitivity & Chemoresistance Assays (L37628) • **Testing performed in AL, GA, TN, VA, WV, SC, NC:** Local Coverage Determination (LCD): In Vitro Chemosensitivity & Chemoresistance Assays (L34554) **NOTE:** See "Policy Guidelines" about investigational services and medical necessity for Medicare. **NOTE:** The above LCD is the primary source of criteria/guidance for CSRAs. However, additional information regarding some chemosensitivity / chemoresistance assays can also be found in the LCD for *Lab: Special Histochemical Stains and Immunohistochemical Stains* (L36353), specifically in the section for "IHC for Chemosensitivity and Resistance Tumor Profiling."

Medicare Coverage Criteria: "MA organizations may create publicly accessible internal coverage criteria… when coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs." *(§ 422.101(b)(6) – see Policy Guidelines below*) • **Medicare Coverage Manuals:** Medicare does not have criteria for chemosensitivity or chemoresistance assays (CSRAs) in a coverage manual. • **National Coverage Determination (NCD):** Medicare does not have an NCD for CSRAs. • **Noridian J-F Local Coverage Determination (LCD)/Local Coverage Article (LCA):** As of the most recent policy review, the Medicare Administrative Contractor (MAC) for Pennsylvania (Novitas) does not have an active LCD for ChemoFX®. • Therefore, in the absence of established Medicare coverage criteria in a manual, NCD, LCD, or other regulatory guidance for the health plan's service area, Company criteria below are applied for medical necessity decision-making.	
ChemoFX®, performed by Helomics [previously Precision Therapeutics, Inc.], in Pittsburgh, PA	Company medical policy for Chemoresistance and Chemosensitivity Assays I. This service is considered **not medically necessary** for Medicare based on the Company medical policy. *See Policy Guidelines below.*

IMPORTANT NOTICE: While some services or items may appear medically indicated for an individual, they may also be a direct exclusion of Medicare or the member's benefit plan. Such excluded services or items by Medicare and member EOCs include, but are not limited to, services or procedures considered to be cosmetic, not medical in nature, or those considered not medically reasonable or necessary under *Title XVIII of the Social Security Act, §1862(a)(1)(A).* If there is uncertainty regarding coverage of a service or item, please review the member EOC or submit a pre-service organization determination request. Note that the Medicare Advance Beneficiary Notice of Noncoverage (ABN) form **cannot** be used for Medicare Advantage members. *(Medicare Advance Written Notices of Non-coverage. MLN006266 May 2021)*

POLICY CROSS REFERENCES

None

The full Company portfolio of Medicare Medical Policies is available online and can be accessed here.

POLICY GUIDELINES

MEDICARE AND MEDICAL NECESSITY

Only medically reasonable and necessary services or items which treat illness or injury are eligible for Medicare coverage, as outlined in *Title XVIII of the Social Security Act, §1862(a)(1)(A)*.

Diagnostic Laboratory Test Jurisdiction

The Company policy PHA Medicare Medical Policy Development and Application (MP50) describes the Plan's hierarchy with respect to Medicare medical policy development. In compliance with Medicare guidelines, some LCDs and LCAs used may be for test service areas outside of the Company service area. This is because Medicare's general rule regarding jurisdiction of claims furnished by an independent laboratory is that jurisdiction lies with the A/B MAC (B) (aka, Medicare Contractor) serving the area in

which the laboratory test is performed.[1]

Services Considered "Investigational" Within an LCD

Services which lack scientific evidence regarding safety and efficacy because they are investigational are "not medically reasonable or necessary" for Medicare Plan members. *(Medicare Claims Processing Manual, Ch. 23, §30 A)*

Services Without a Specific NCD or LCD

The ChemoFX® assay ***used to*** be addressed by an LCD by the MAC with jurisdiction over the performing laboratory (Novitas Solutions), which was the LCD for *In Vitro Chemosensitivity & Chemoresistance Assays* (L36634). While it was effective, this LCD read, "Novitas Solutions considers tumor chemosensitivity and chemoresistance assays (CSRAs) experimental and investigational as there has been insufficient evidence to support that these assays influence treatment options and improved clinical outcomes."

However, Novitas retired this LCD effective 7/1/2020[2] and thus, there is no longer a Medicare-based coverage policy for this testing.

MA organizations (MAOs) make medical necessity determinations based on coverage and benefit criteria, current standards of care, the member's unique personal medical history (e.g., diagnoses, conditions, functional status, co-morbidities, etc.), physician recommendations, and clinical notes, as well as involvement of a plan medical director, where appropriate. *(§ 422.101(c)(1))*

> "MA organizations may create publicly accessible internal coverage criteria that are based on current evidence in widely used treatment guidelines or clinical literature when coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs. Current, widely-used treatment guidelines are those developed by organizations representing clinical medical specialties, and refers to guidelines for the treatment of specific diseases or conditions. Acceptable clinical literature includes large, randomized controlled trials or prospective cohort studies with clear results, published in a peer-reviewed journal, and specifically designed to answer the relevant clinical question, or large systematic reviews or meta-analyses summarizing the literature of the specific clinical question." *(§ 422.101(b)(6) and Medicare Managed Care Manual, Ch. 4, §90.5*

The Company policy for *PHA Medicare Medical Policy Development and Application* (MP50) provides details regarding Medicare's definition of medical necessity and the hierarchy of Medicare references and resources during the development of medical policies, as well as the Plan's use of evidence-based processes for policy development. The Company medical policy for ChemoFX® will apply to Medicare Advantage plan members, and is consistent with the previous non-coverage position found in the now-retired Novitas LCD.

REGULATORY STATUS

U.S. FOOD & DRUG ADMINISTRATION (FDA)

While clearance by the Food and Drug Administration (FDA) is a prerequisite for Medicare coverage, the 510(k) premarket clearance process does not in itself establish medical necessity. Medicare payment policy is determined by the interaction of numerous requirements, including but not limited to, the availability of a Medicare benefit category and other statutory requirements, coding and pricing guidelines, as well as national and local coverage determinations and clinical evidence.

BILLING GUIDELINES AND CODING

GENERAL

See associated local coverage articles (LCAs) for related billing and coding guidance:

- LCA: Billing and Coding: In Vitro Chemosensitivity & Chemoresistance Assays (A56073)
- LCA: Billing and Coding: Lab: Special Histochemical Stains and Immunohistochemical Stains (A57614)

CODES*		
CPT	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 *(Use for Onco4D™, by Animated Dynamics Inc.)*
	0248U	Oncology, spheroid cell culture in 3D microenvironment, 12 drug panel, brain- or brain metastasis-response prediction for each drug *(Use for the 3D Predict Glioma test, by KIYATEC® Inc.)*
	~~0564T~~	**TERMED 12/31/2024** ~~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 *(Use for ChemoID)*~~
	0435U	Oncology, chemotherapeutic drug cytotoxicity assay of cancer stem cells (CSCs), from cultured CSCs and primary tumor cells, categorical drug response reported based on cytotoxicity percentage observed, minimum of 14 drugs or drug combinations *(Use for ChemoID)*
	0525U	Oncology, spheroid cell culture, 11-drug panel (carboplatin, docetaxel, doxorubicin, etoposide, gemcitabine, niraparib, olaparib, paclitaxel, rucaparib, topotecan, veliparib) ovarian, fallopian, or peritoneal response prediction for each drug *(Use for the 3D Predict™ Ovarian test, by KIYATEC® Inc.)*
	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)
	86849	Tissue Typing Immunological Procedures
	87999	Unlisted microbiology procedure
	88299	Unlisted cytogenetic study
	89240	Unlisted miscellaneous pathology test
HCPCS	None	

***Coding Notes:**

- The code list above is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit. According to Medicare, "presence of a payment amount in the MPFS and the Medicare physician fee schedule database (MPFSDB) does not imply that CMS has determined that the service may be covered by Medicare." The issuance of a CPT or HCPCS code or the provision of a payment or fee amount by Medicare does **not** make a procedure medically reasonable or necessary or a covered benefit by Medicare. *(Medicare Claims Processing Manual, Chapter 23 - Fee Schedule Administration and Coding Requirements, §30 - Services Paid Under the Medicare Physician's Fee Schedule, A. Physician's Services)*
- All unlisted codes are reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is submitted for non-covered services addressed in this policy then it will be **denied as not covered**. If an unlisted code is submitted for potentially covered services addressed in this policy, to avoid post-service denial, **prior authorization is recommended**.
- **See the non-covered and prior authorization lists on the Company Medical Policy, Reimbursement Policy, Pharmacy Policy and Provider Information website for additional information.**
- HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as "medically unlikely edits" (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

REFERENCES

1. Medicare Claims Processing Manual, Chapter 16 - Laboratory Services, §50.5 - Jurisdiction of Laboratory Claims; Available at: https://www.cms.gov/regulations-and-guidance/guidance/manuals/downloads/clm104c16.pdf. Accessed 3/28/2024.
2. Medicare Coverage Database (MCD) Archive web site; Available at: https://localcoverage.cms.gov/mcd_archive/search.aspx?clickon=search. Accessed 3/28/2024.

POLICY REVISION HISTORY

DATE	REVISION SUMMARY
7/2022	New Medicare Advantage medical policy (converted to new format 2/2023)
4/2023	Q2 2023 code update (termed codes 0324U and 0325U)
8/2023	Annual review, no change to criteria, but language revision due to Company policy change from "investigational" to "not medically necessary"
1/2024	Q1 2024 code updates
6/2024	Annual review, no change to criteria
10/2024	Q4 2024 code updates