DRAFT Medical Coverage Policy | Multicancer Early Detection Testing

EFFECTIVE DATE: 01|01|2024
POLICY LAST UPDATED: 10|02|2023

OVERVIEW
Many cancers appear to have a better prognosis if diagnosed early in their natural history. This has led to efforts to detect preclinical cancers in asymptomatic individuals through screening. Cancer screening tests such as 'liquid biopsies' that are minimally invasive and can simultaneously detect multiple types of cancer have been called multicancer early detection (MCED) tests.

MEDICAL CRITERIA
Not applicable

PRIOR AUTHORIZATION
Prior authorization is necessary

POLICY STATEMENT
Medicare Advantage Plans
The use of multicancer early detection (MCED) tests (e.g., Galleri) is not covered for cancer screening as the evidence is insufficient to determine that the technology results in an improvement in net health outcome.

Commercial Products
The use of multicancer early detection (MCED) tests (e.g., Galleri) is not medically necessary as the evidence is insufficient to determine that the technology results in an improvement in net health outcome.

Some genetic testing services are not covered and a contract exclusion for any self-funded group that has excluded the expanded coverage of biomarker testing related to the state mandate, R.I.G.L**. §27-19-81** described in the Biomarker Testing Mandate policy. For these groups, a list of which genetic testing services are covered with prior authorization, are not medically necessary or are not covered because they are a contract exclusion can be found in the Coding section of the Genetic Testing Services or Proprietary Laboratory Analyses policies. Please refer to the appropriate Benefit Booklet to determine whether the member's plan has customized benefit coverage. Please refer to the list of Related Policies for more information.

COVERAGE
Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for applicable not medically necessary/not covered benefits/coverage.

BACKGROUND
Cancer is the second leading cause of death in the US following heart disease. Cancer is the cause of death in 1 of every 5 deaths in the US. In the US, more than 1.7 million new cases of cancer were reported in 2019, and almost 600,000 people died of cancer.

Many cancers appear to have a better prognosis if diagnosed early in their natural history. This has led to efforts to detect preclinical cancers in asymptomatic persons through screening. However, screening tests have associated benefits and harms that must be considered when evaluating whether a test should be used in a population.

Early detection of cancer has 2 components: early diagnosis and screening. Early diagnosis is the early identification of cancer in *symptomatic* individuals with the aim of reducing the proportion of individuals

diagnosed at a late stage. Screening is the identification of preclinical cancer or precursor lesions in apparently healthy, *asymptomatic* populations by tests that can be applied rapidly and widely in the target population. This review focuses on tests for screening indications.

Cancer screening tests such as 'liquid biopsies' that are minimally invasive and can simultaneously detect multiple types of cancer have been called multicancer early detection (MCED) tests.

No MCED tests have been approved or cleared by the U.S. Food and Drug Administration (FDA). GRAIL, Inc. announced in 2019 that its MCED test (Galleri®) had been granted breakthrough device designation by the FDA.

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. Galleri is available under the auspices of the Clinical Laboratory Improvement Amendments.

Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the FDA has chosen not to require any regulatory review of this test.

For individuals who are being screened for cancer who receive multicancer early detection (MCED) testing with Galleri, the published evidence includes case-control studies. Relevant outcomes are overall survival, disease-specific survival, functional outcomes, quality of life, treatment-related mortality, and treatment-related morbidity. Specifics of how the test should be used in practice, including the appropriate at-risk target populations, frequency of testing, and follow-up of positive and negative test results, have not been fully described. Performance characteristics for both the prediction of overall likelihood of cancer and the tissue of origin are needed. Published clinical validity studies have used populations consisting of patients with an established diagnosis of cancer and control populations of healthy individuals and as such, do not reflect the intended-use population. Therefore, estimates of sensitivity, specificity, false-positives, false-negatives and predictive values are not available for the intended-use population. No clinical utility studies have been published; estimates of changes in cancer-specific mortality, quality of life, functional outcomes and rates of overdiagnosis and overtreatment are unknown. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

CODING

Medicare Advantage Plans and Commercial Products

CPT codes have not been assigned to the test(s) addressed in this policy. Therefore, an Unlisted code(s) should be used.

RELATED POLICIES

Biomarker Testing Mandate
Genetic Testing Services
Proprietary Laboratory Analysis (PLA)
Unlisted Procedures

PUBLISHED

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REFERENCES

1. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National CancerInstitute. U.S. Cancer Statistics Data Visualizations Tool, based on 2021 submission data (1999-2019).https://www.cdc.gov/cancer/dataviz. Accessed April 12, 2023.

2. World Health Organization. Screening and early detection. https://www.who.int/europe/news-room/fact-sheets/item/cancer-screening-and-early-detection-of-cancer. Accessed April 12, 2023.
3. GRAIL, LLC. GRAIL Announces Significant Progress with Multi-Cancer Early Detection Test Including FDA BreakthroughDevice Designation. https://grail.com/press-releases/grail-announces-significant-progress-with-multi-cancer-early-detection-test-including-fda-breakthrough-device-designation/. Accessed April 12, 2023.
4. Bossuyt PM, Irwig L, Craig J, et al. Comparative accuracy: assessing new tests against existing diagnostic pathways.BMJ. May 06 2006; 332(7549): 1089-92. PMID 16675820
5. Cancer.Net Editorial Board. Understanding Cancer Risk. 2018; https://www.cancer.net/navigating-cancer-care/prevention-and-healthy-living/understanding-cancer-risk. Accessed April 12, 2023.
6. Siegel RL, Miller KD, Fuchs HE, et al. Cancer statistics, 2022. CA Cancer J Clin. Jan 2022; 72(1): 7-33. PMID 35020204
7. Minasian LM, Pinsky P, Katki HA, et al. Study design considerations for trials to evaluate multicancer early detectionassays for clinical utility. J Natl Cancer Inst. Mar 09 2023; 115(3): 250-257. PMID 36458902
8. GRAIL, LLC. Frequently asked questions for healthcare providers interested in ordering the Galleri test.https://www.galleri.com/hcp/support/provider-faqs. Accessed April 12, 2023.
9. Jamshidi A, Liu MC, Klein EA, et al. Evaluation of cell-free DNA approaches for multi-cancer early detection. Cancer Cell.Dec 12 2022; 40(12): 1537-1549.e12. PMID 36400018
10. Liu MC, Oxnard GR, Klein EA, et al. Sensitive and specific multi-cancer detection and localization using methylationsignatures in cell-free DNA. Ann Oncol. Jun 2020; 31(6): 745-759. PMID 33506766
11. Duffy MJ, Diamandis EP, Crown J. Circulating tumor DNA (ctDNA) as a pan-cancer screening test: is it finally on thehorizon?. Clin Chem Lab Med. Jul 27 2021; 59(8): 1353-1361. PMID 33856748
12. Cuzick J, Cafferty FH, Edwards R, et al. Surrogate endpoints for cancer screening trials: general principles and anillustration using the UK Flexible Sigmoidoscopy Screening Trial. J Med Screen. 2007; 14(4): 178-85. PMID 18078562
13. Menon U, Gentry-Maharaj A, Burnell M, et al. Ovarian cancer population screening and mortality after long-term follow-upin the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS): a randomised controlled trial. Lancet. Jun 052021; 397(10290): 2182-2193. PMID 33991479
14. Owens L, Gulati R, Etzioni R. Stage Shift as an Endpoint in Cancer Screening Trials: Implications for EvaluatingMulticancer Early Detection Tests. Cancer Epidemiol Biomarkers Prev. Jul 01 2022; 31(7): 1298-1304. PMID 35477176
15. Klein EA, Richards D, Cohn A, et al. Clinical validation of a targeted methylation-based multi-cancer early detection testusing an independent validation set. Ann Oncol. Sep 2021; 32(9): 1167-1177. PMID 34176681
16. Tang WHW, Yimer H, Tummala M, et al. Performance of a targeted methylation-based multi-cancer early detection test byrace and ethnicity. Prev Med. Feb 2023; 167: 107384. PMID 36495927
17. Shao SH, Allen B, Clement J, et al. Multi-cancer early detection test sensitivity for cancers with and without currentpopulation-level screening options. Tumori. Oct 31 2022: 3008916221133136. PMID 36316952
18. Neal RD, Johnson P, Clarke CA, et al. Cell-Free DNA-Based Multi-Cancer Early Detection Test in an AsymptomaticScreening Population (NHS-Galleri): Design of a Pragmatic, Prospective Randomised Controlled Trial. Cancers (Basel).Oct 01 2022; 14(19). PMID 36230741
19. National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic;Version 3.2023. https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf. Accessed April 12, 2023.

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