**Medical Coverage Policy |** Germline and Somatic Biomarker Testing (Including Liquid Biopsy) for Targeted Treatment and Immunotherapy in Breast Cancer

**EFFECTIVE DATE:** 01|01|2024
**POLICY LAST REVIEWED:** 09|06|2023

## OVERVIEW

Multiple biomarkers are being evaluated to predict response to targeted treatments and immunotherapy for patients with advanced or high-risk breast cancer. These include tissue-based testing as well as circulating tumor DNA and circulating tumor cell testing (known as liquid biopsy).

The following tests are addressed in this policy:

- Therascreen PIK3CA (QIAGEN Sciences) CPT code 0155U
- Therascreen® PIK3CA RGQ PCR Kit (QIAGEN Sciences) CPT code 0177U

## MEDICAL CRITERIA

**Medicare Advantage Plans and Commercial Products**

PIK3CA testing may be medically necessary to predict treatment response to alpelisib (Piqray) in individuals with hormone receptor-positive, HER2-negative advanced or metastatic breast cancer who have progressed on or after an endocrine-based regimen.

- When tumor tissue is available, use of tissue for testing is preferred but is not required.

## PRIOR AUTHORIZATION

**Medicare Advantage Plans and Commercial Products**

Prior authorization is required for Medicare Advantage Plans and recommended for Commercial Products via the online tool for participating providers. See the Related Policies section.

## POLICY STATEMENT

**Medicare Advantage Plans and Commercial Products**

PIK3CA testing may be considered medically necessary when the medical criteria above is met.

PIK3CA testing of tissue in individuals with breast cancer in all other situations is considered not covered for Medicare Advantage Plans and not medically necessary for Commercial Products as the evidence is insufficient to determine the effects of the technology on health outcomes.

**Commercial Products**

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 not medically necessary/not covered laboratory benefits/coverage.

## BACKGROUND

Alterations in the protein coding gene PIK3CA (Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Alpha) occur in approximately 40% of patients with hormone receptor (HR)-positive, HER2-negative breast cancer.
U.S. FDA approved companion diagnostic tests for alpelisib in patients with PIK3CA-mutated breast cancer include both tissue-based and liquid biopsy assays. These tests are approved to measure 11 variants in the PIK3CA gene.

For individuals with hormone receptor-positive, HER2-negative advanced or metastatic breast cancer who receive PIK3CA gene testing to select targeted treatment, the evidence includes a randomized, placebo-controlled trial of alpelisib compared to placebo in men and postmenopausal women with advanced breast cancer who had previously received endocrine therapy. Relevant outcomes include overall survival, disease-specific survival, test validity, quality of life, and treatment-related morbidity. Among patients with PIK3C A-positive tumors who received targeted therapy, PFS was 11.0 months (95% CI, 7.5 to 14.5), compared to 5.7months (95% CI, 3.7 to 7.4) in PIK3CA-positive patients who received standard care. In contrast, the hazard ratio for PFS in the cohort without PIK3CA-mutated cancer was not significantly different for the active versus placebo groups. The overall response rate was higher in patients with PIK3CA-positive tumors compared to the rate in the standard care group (26.6% [95% CI 20.1 to 34.0] vs. 12.8% [95% CI, 8.2 to 18.7]). The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

## CODING

**Medicare Advantage Plans and Commercial Products**

The following CPT code(s) are medically necessary when the medical criteria, above, is met.

**0155U** Oncology (breast cancer), DNA, PIK3CA (phosphatidylinositol-4,5-bisphosphate 3- kinase, catalytic subunit alpha) (eg, breast cancer) gene analysis (ie, p.C420R, p.E542K, p.E545A,p.E545D [g.1635G>T only], p.E545G, p.E545K, p.Q546E, p.Q546R, p.H1047L, p.H1047R,p.H1047Y), utilizing formalin-fixed paraffin-embedded breast tumor tissue, reported as PIK3CA gene mutation status (PLA code for the therascreen® PIK3CA RGQ PCR Kit from QIAGEN)

**0177U** Oncology (breast cancer), DNA, PIK3CA (phosphatidylinositol-4,5-bisphosphate 3-kinasecatalytic subunit alpha) gene analysis of 11 gene variants utilizing plasma, reported asPIK3CA gene mutation status (PLA code for the therascreen® PIK3CA RGQ PCR Kit test from QIAGEN)

## RELATED POLICIES

Biomarker Testing Mandate
Proprietary Laboratory Analysis (PLA)

## PUBLISHED

Provider Update, November 2023

## REFERENCES


1. Winchester DP. Breast cancer in young women. Surg Clin North Am. Apr 1996; 76(2): 279-87. PMID8610264
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3. U.S. Food & Drug Administration. Drugs@FDA: FDA-Approved Drugs. https://www.accessdata.fda.gov/scripts/cder/daf/. Accessed November 1, 2022.
4. Andre F, Ciruelos E, Rubovszky G, et al. Alpelisib for PIK3CA -Mutated, Hormone Receptor-Positive Advanced Breast Cancer. N Engl J Med. May 16 2019; 380(20): 1929-1940. PMID 31091374
5. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Breast Cancer. Version 4, 2022. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed October 24, 2022.

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