**Indication**
PIQRAY is indicated in combination with fulvestrant for the treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, PIK3CA-mutated, advanced or metastatic breast cancer as detected by an FDA-approved test following progression on or after an endocrine-based regimen.

**Important Safety Information**
PIQRAY is contraindicated in patients with severe hypersensitivity to it or any of its components.

**Severe Hypersensitivity:** Severe hypersensitivity reactions, including anaphylaxis and anaphylactic shock, can occur in patients treated with PIQRAY. Severe hypersensitivity reactions were manifested by symptoms including, but not limited to, dyspnea, flushing, rash, fever, or tachycardia. The incidence of grade 3 and 4 hypersensitivity reactions was 0.7%. Angioedema has been reported in the postmarketing setting in patients treated with PIQRAY. Advise patients of the signs and symptoms of severe hypersensitivity reactions. Permanently discontinue PIQRAY in the event of severe hypersensitivity.

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**Your guide to navigating PIK3CA mutation testing**

**Why to test?**

**When to test?**

**How to test?**

**Single-gene testing (PCR)**

**Multi-gene testing (NGS)**

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Please see additional Important Safety Information throughout and on pages 11-12. Please [click here](#) for full Prescribing Information.
Patients with a PIK3CA mutation face a worse prognosis\(^2\)

- PIK3CA mutations have been identified in patients with endocrine resistance\(^3,4\)

Knowledge of PIK3CA mutation status can inform up-front treatment planning for appropriate patients

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Important Safety Information (cont)

**Severe Cutaneous Adverse Reactions (SCARs):** SCARs, including Stevens-Johnson syndrome (SJS), erythema multiforme (EM), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) can occur in patients treated with PIQRAY. In the SOLAR-1 study, SJS and EM were reported in 0.4% and 1.1% of patients, respectively. DRESS was reported in patients in the postmarketing setting. If signs or symptoms of SCARs occur, interrupt PIQRAY until the etiology of the reaction has been determined. Consultation with a dermatologist is recommended.

Please see additional Important Safety Information throughout and on pages 11-12. Please [click here](#) for full Prescribing Information.
Why to test?

Test for PIK3CA mutations at initial MBC diagnosis if tumor is HR+/HER2- *

+ Following progression on or after an endocrine-based regimen.

When to test?

+ Following progression on or after an endocrine-based regimen.

How to test?

Tumor tissue biopsy

- Positive for PIK3CA mutation
  - Alpelisib + fulvestrant

- Negative for PIK3CA mutation
  - Test tumor tissue

Liquid biopsy

- Positive for PIK3CA mutation
  - Alpelisib + fulvestrant

- Negative for PIK3CA mutation

Per NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®), assess for PIK3CA mutation as part of the initial MBC workup if all of the following are true5:

- Patient has recurrent/Stage IV (M1) disease
- Tumor is HR+/HER2-
- Considering therapy with alpelisib + fulvestrant

PIQRAY is indicated for postmenopausal women, and men, with HR+/HER2-, PIK3CA-mutated, advanced or metastatic breast cancer (aBC or MBC), in combination with fulvestrant following progression on or after an endocrine-based regimen.

MBC, metastatic breast cancer.

+ Following progression on or after an endocrine-based regimen.

If liquid biopsy is negative, tumor tissue testing is recommended.

‡ The safety of alpelisib in patients with type 1 or uncontrolled type 2 diabetes has not been established.

§ Unless a recurrence or unmanageable toxicity occurs, per HR+/HER2- MBC American Society of Clinical Oncology® Guideline Update 2021.

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Important Safety Information (cont)

Severe Cutaneous Adverse Reactions (SCARs) (cont): If a SCAR is confirmed, permanently discontinue PIQRAY. Do not reintroduce PIQRAY in patients who have experienced previous SCARs during PIQRAY treatment. If it is not confirmed, PIQRAY may require dose modifications, topical corticosteroids, or oral antihistamine treatment.

Advise patients of the signs and symptoms of SCARs (eg, a prodrome of fever, flu-like symptoms, mucosal lesions, progressive skin rash, or lymphadenopathy).

Please see additional Important Safety Information throughout and on pages 11-12. Please click here for full Prescribing Information.
PIK3CA mutations can be detected in tissue or plasma specimens

- PIK3CA mutations are generally stable; therefore, archival specimens and recent or new biopsies can be tested.
- If no mutation is detected in a plasma specimen, retest the patient using tumor tissue. Click here to learn more.

Tumor tissue
PIK3CA mutations can be detected in primary tumors or metastatic sites.

Plasma
PIK3CA mutations can be detected in peripheral whole blood.

The PIK3CA mutation companion diagnostic tests for PIQRAY include 11 different mutations in the PIK3CA gene as part of the FDA-approved indication.

- These are among the most common PIK3CA mutations in breast cancer and were assessed at screening to enroll in the PIK3CA mutant cohort in the SOLAR-1 trial.

Important Safety Information (cont)

Hyperglycemia: Severe hyperglycemia, in some cases associated with hyperglycemic hyperosmolar non-ketotic syndrome (HHNKS) or ketoacidosis has occurred in patients treated with PIQRAY. Fatal cases of ketoacidosis have occurred in the postmarketing setting.

Hyperglycemia was reported in 65% of patients treated with PIQRAY. Grade 3 (FPG >250-500 mg/dL) and grade 4 (FPG >500 mg/dL) hyperglycemia were reported in 33% and 3.9% of patients, respectively. Ketoacidosis was reported in 0.7% of patients (n=2) treated with PIQRAY.

Please see additional Important Safety Information throughout and on pages 11-12. Please click here for full Prescribing Information.
How to test (cont)

Negative results for PIK3CA mutation using plasma require further investigation

Multiple factors may contribute to false negatives in plasma testing\(^7,11,12\)

- **Biological differences in plasma testing**
- **Specimen handling**
- **QIAGEN companion diagnostic (CDx) differences in plasma and tissue in SOLAR-1**

- Tumors in cancer types that have low-level DNA shedding may result in false negatives in plasma testing\(^11\)
- Specimen handling can lead to additional false negatives when using plasma-based tests\(^12\)

44% of patients (140/317)

If PIK3CA mutation is not detected in plasma, **retest the patient using tumor tissue**\(^7\)

Important Safety Information (cont)

**Hyperglycemia (cont):** Before initiating treatment with PIQRAY, test fasting plasma glucose (FPG), HbA1c, and optimize blood glucose. After initiating treatment, monitor fasting glucose (FPG or fasting blood glucose) at least once every week for the first 2 weeks, then at least once every 4 weeks, and as clinically indicated. Monitor HbA1c every 3 months and as clinically indicated. Monitor fasting glucose more frequently for the first few weeks during treatment in patients with risk factors for hyperglycemia such as obesity (BMI ≥30), elevated FPG, HbA1c at the upper limit of normal or above, use of concomitant systemic corticosteroids, or age ≥75.

If a patient experiences hyperglycemia after initiating treatment, monitor fasting glucose as clinically indicated, and at least twice weekly until fasting glucose decreases to normal levels. During treatment with anti-hyperglycemic medication, continue monitoring fasting glucose at least once a week for 8 weeks, followed by once every 2 weeks and as clinically indicated. Consider consultation with a health care practitioner with expertise in the treatment of hyperglycemia and counsel patients on lifestyle changes.

Please see additional Important Safety Information throughout and on pages 11-12. Please [click here](#) for full Prescribing Information.
Access the PIK3CA Mutation CDx Testing Program

NeoGenomics Laboratories will conduct tumor tissue and plasma testing using the QIAGEN therascreen® PIK3CA RGQ PCR Kit.® Appropriate patients may receive one tumor tissue or plasma PIK3CA mutation test at no cost for the purpose of determining whether or not the patient has a PIK3CA mutation and is eligible for alpelisib for an FDA-approved indication, without regard to purchase of any prescribed drug or any other product. If the patient tests negative for PIK3CA mutation using plasma, eligible patients may also receive one PIK3CA reflex tissue test at no cost. No patient, health care program, or beneficiary shall be billed for this mutation test. The test shall not be included in a bundled payment to any health care facility including, but not limited to, a hospital. The ordering physician shall not be compensated any fees in connection with this mutation testing, such as for specimen collection, handling, or data reporting. Program is not valid where prohibited by law. Novartis reserves the right to rescind, revoke, or amend the program without notice. If no mutation is detected in a plasma specimen, confirm with a tumor tissue reflex test.

Get the Ordering Guide

Have you received your PIK3CA CDx Testing Program Ordering Guide? Reach out to your Novartis Specialist using the contact information on page 10 of this brochure.

FDA-approved single-gene tissue and plasma testing

QIAGEN therascreen® PIK3CA RGQ PCR Kit

PIK3CA mutation testing is available to appropriate patients at no cost

- Information on FDA-approved tests for the detection of PIK3CA mutations in breast cancer is available at [www.fda.gov/companiondiagnostics](http://www.fda.gov/companiondiagnostics)

therascreen is a registered trademark of QIAGEN group.

Important Safety Information (cont)

Hyperglycemia (cont): The safety of PIQRAY in patients with type 1 and uncontrolled type 2 diabetes has not been established as these patients were excluded from the SOLAR-1 trial. Patients with a medical history of controlled type 2 diabetes were included. Patients with a history of diabetes mellitus may require intensified hyperglycemic treatment. Closely monitor patients with diabetes. Based on the severity of the hyperglycemia, PIQRAY may require dose interruption, reduction, or discontinuation. Advise patients of the signs and symptoms of hyperglycemia (eg, excessive thirst, urinating more often than usual or higher amount of urine than usual, or increased appetite with weight loss).

Please see additional Important Safety Information throughout and on pages 11-12. Please click here for full Prescribing Information.
Why to test?

When to test?

How to test?

Single-gene testing (PCR)

Multi-gene testing (NGS)

Key contacts

Important Safety Information

**Single-gene testing (PCR) (cont)**

**FFPE tissue**

Breast tumor tissue (either primary or metastatic) is required; non-breast tumors are not accepted for this test. Paraffin block is preferred. Alternatively, send 1 H&E slide plus 6-12 unstained slides for core needle biopsy (or 5-10 slides for resection) cut at 5 microns. Please use positively charged slides and 10% NBF fixative. Do not use zinc fixatives. Decalcified specimens are not accepted.¹³

**Peripheral blood**

Please contact Client Services at 1-866-776-5907, option 3, to review special collection and handling requirements and to receive the test request form and shipping supplies.

**Turnaround time**

NeoGenomics generally expects to provide results within 1 week of specimen receipt.

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**Important Safety Information (cont)**

**Pneumonitis:** Severe pneumonitis, including acute interstitial pneumonitis and interstitial lung disease, can occur in patients treated with PIQRAY. Pneumonitis was reported in 1.8% of patients treated with PIQRAY.

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**PIK3CA Mutation CDx findings using NeoGenomics PCR are found on the first page of the report**

To find alternate labs that have verified the QIAGEN *therascreen* PIK3CA RGQ PCR Kit, visit QIAGEN.com/PIK3CA-lab-finder or call 1-800-362-7737

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Please see additional Important Safety Information throughout and on pages 11-12. Please click here for full Prescribing Information.
Multi-gene testing (NGS)

FDA-approved multi-gene tissue and plasma testing

FoundationOne®CDx and FoundationOne®Liquid CDx are covered by Original Medicare and Medicare Advantage for qualifying beneficiaries

Foundation Medicine offers in-home blood draw with mobile phlebotomy through its partner, ExamOne®, to support broader access to FoundationOne®Liquid CDx, at no additional cost

Information on FDA-approved tests for the detection of PIK3CA mutations in breast cancer is available at www.fda.gov/companiondiagnostics

Novartis is not responsible for any such third party content that may be accessed via the above provided resources. Novartis does not endorse the content contained in these sites, nor the organizations publishing those sites, and hereby disclaims any responsibility for such content.

Foundation Medicine, FoundationOne CDx, and FoundationOne Liquid CDx are registered trademarks of Foundation Medicine, Inc. ExamOne is a registered trademark of Quest Diagnostics.

Important Safety Information (cont)

Pneumonitis (cont): In patients who have new or worsening respiratory symptoms or are suspected to have developed pneumonitis, interrupt PIQRAY immediately and evaluate the patient for pneumonitis. Consider a diagnosis of noninfectious pneumonitis in patients presenting with nonspecific respiratory signs and symptoms such as hypoxia, cough, dyspnea, or interstitial infiltrates on radiologic exams and in whom infectious, neoplastic, and other causes have been excluded by means of appropriate investigations. Permanently discontinue PIQRAY in all patients with confirmed pneumonitis. Advise patients to immediately report new or worsening respiratory symptoms.

Please see additional Important Safety Information throughout and on pages 11-12. Please click here for full Prescribing Information.
Multi-gene testing (NGS) (cont)

CDx for tissue testing results

CDx for blood testing results

FoundationOne®CDx uses DNA isolated from FFPE tumor tissue specimens. When feasible, please send FFPE tissue block + 1 H&E slide OR 10 unstained slides (positively charged and unbaked at 4-5 microns thick) + 1 H&E slide.9

FoundationOne®Liquid CDx uses two tubes of peripheral whole blood (8.5 mL per tube).9

Foundation Medicine generally expects to provide results in 12 days or less from specimen receipt.

Important Safety Information (cont)

Diarrhea or Colitis: Severe diarrhea, resulting in dehydration and in some cases in acute kidney injury, can occur in patients treated with PIQRAY. Most patients (58%) experienced diarrhea during treatment with PIQRAY. Grade 3 diarrhea occurred in 7% (n=19) of patients. Colitis has been reported in the postmarketing setting in patients treated with PIQRAY. Monitor patients for diarrhea and additional symptoms of colitis, such as abdominal pain and mucus, or blood in the stool. Based on the severity of the diarrhea or colitis, PIQRAY may require dose interruption, reduction, or discontinuation. Advise patients to start antidiarrheal treatment, increase oral fluids, and notify their health care provider if diarrhea occurs while taking PIQRAY. For patients with colitis, additional treatment, such as enteric-acting and/or systemic steroids, may be required.

Please see additional Important Safety Information throughout and on pages 11-12. Please click here for full Prescribing Information.
Key contacts

NeoGenomics Laboratories
Client Services
neogenomics.com/pik3ca
Order online through NeoLINK® at neolink.neogenomics.com
1-866-776-5907

Foundation Medicine
Order online through foundationmedicine.com/order
Call Client Services at 1-888-988-3639

QIAGEN Lab Finder
QIAGEN.com/PIK3CA-lab-finder
1-800-362-7737

Novartis Specialist
hcp.novartis.com/contact

PIK3CA Testing Navigator
For detailed testing information, visit our comprehensive PIK3CA Testing Navigator at PIK3CA-Testing.com

Learn more about PIK3CA mutation testing

NeoLINK is a registered trademark of NeoGenomics Laboratories, Inc.

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**Indication**
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If a SCAR is confirmed, permanently discontinue PIQRAY. Do not reintroduce PIQRAY in patients who have experienced previous SCARs during PIQRAY treatment. If it is not confirmed, PIQRAY may require dose modifications, topical corticosteroids, or oral antihistamine treatment.

Advise patients of the signs and symptoms of SCARs (eg, a prodrome of fever, flu-like symptoms, mucosal lesions, progressive skin rash, or lymphadenopathy).

**Hyperglycemia:** Severe hyperglycemia, in some cases associated with hyperglycemic hyperosmolar non-ketotic syndrome (HHNKs) or ketoacidosis has occurred in patients treated with PIQRAY. Fatal cases of ketoacidosis have occurred in the postmarketing setting.

Hyperglycemia was reported in 65% of patients treated with PIQRAY. Grade 3 (FPG >250-500 mg/dL) and grade 4 (FPG >500 mg/dL) hyperglycemia were reported in 33% and 3.9% of patients, respectively. Ketoacidosis was reported in 0.7% of patients (n=2) treated with PIQRAY.

Before initiating treatment with PIQRAY, test fasting plasma glucose (FPG), HbA1c, and optimize blood glucose. After initiating treatment, monitor fasting glucose (FPG or fasting blood glucose) at least once every week for the first 2 weeks, then at least once every 4 weeks, and as clinically indicated. Monitor HbA1c every 3 months and as clinically indicated. Monitor fasting glucose more frequently for the first few weeks during treatment in patients with risk factors for hyperglycemia such as obesity (BMI ≥30), elevated FPG, HbA1c at the upper limit of normal or above, use of concomitant systemic corticosteroids, or age ≥75.

If a patient experiences hyperglycemia after initiating treatment, monitor fasting glucose as clinically indicated, and at least twice weekly until fasting glucose decreases to normal levels. During treatment with anti-hyperglycemic medication, continue monitoring fasting glucose at least once a week for 8 weeks, followed by once every 2 weeks and as clinically indicated. Consider consultation with a health care practitioner with expertise in the treatment of hyperglycemia and counsel patients on lifestyle changes.

The safety of PIQRAY in patients with type 1 and uncontrolled type 2 diabetes has not been established as these patients were excluded from the SOLAR-1 trial. Patients with a medical history of controlled type 2 diabetes were included. Patients with a history of diabetes mellitus may require intensified hyperglycemic treatment. Closely monitor patients with diabetes.

Based on the severity of the hyperglycemia, PIQRAY may require dose interruption, reduction, or discontinuation. Advise patients of the signs and symptoms of hyperglycemia (eg, excessive thirst, urinating more often than usual or higher amount of urine than usual, or increased appetite with weight loss).
Important Safety Information (cont)

**Pneumonitis:** Severe pneumonitis, including acute interstitial pneumonitis and interstitial lung disease, can occur in patients treated with PIQRAY. Pneumonitis was reported in 1.8% of patients treated with PIQRAY.

In patients who have new or worsening respiratory symptoms or are suspected to have developed pneumonitis, interrupt PIQRAY immediately and evaluate the patient for pneumonitis. Consider a diagnosis of noninfectious pneumonitis in patients presenting with nonspecific respiratory signs and symptoms such as hypoxia, cough, dyspnea, or interstitial infiltrates on radiologic exams and in whom infectious, neoplastic, and other causes have been excluded by means of appropriate investigations.

Permanently discontinue PIQRAY in all patients with confirmed pneumonitis. Advise patients to immediately report new or worsening respiratory symptoms.

**Diarrhea or Colitis:** Severe diarrhea, resulting in dehydration and in some cases in acute kidney injury, can occur in patients treated with PIQRAY. Most patients (58%) experienced diarrhea during treatment with PIQRAY. Grade 3 diarrhea occurred in 7% (n=19) of patients. Colitis has been reported in the postmarketing setting in patients treated with PIQRAY. Monitor patients for diarrhea and additional symptoms of colitis, such as abdominal pain and mucus, or blood in the stool. Based on the severity of the diarrhea or colitis, PIQRAY may require dose interruption, reduction, or discontinuation. Advise patients to start antidiarrheal treatment, increase oral fluids, and notify their health care provider if diarrhea occurs while taking PIQRAY. For patients with colitis, additional treatment, such as enteric-acting and/or systemic steroids, may be required.

**Embryo-Fetal Toxicity:** Based on findings in animals and its mechanism of action, PIQRAY can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with PIQRAY and for 1 week after the last dose. Advise male patients with female partners of reproductive potential to use condoms and effective contraception during treatment with PIQRAY and for 1 week after the last dose. Refer to the full Prescribing Information of fulvestrant for pregnancy and contraception information.

**The most common adverse reactions (all grades, incidence ≥20%)** were diarrhea (58%), rash (52%), nausea (45%), fatigue (42%), decreased appetite (36%), stomatitis (30%), vomiting (27%), weight decreased (27%), and alopecia (20%). The most common grade 3/4 adverse reactions (incidence ≥2%) were rash (20%), diarrhea (7%), fatigue (5%), weight decreased (3.9%), nausea (2.5%), stomatitis (2.5%), and mucosal inflammation (2.1%).

**The most common laboratory abnormalities (all grades, incidence ≥20%)** were glucose increased (79%), creatinine increased (67%), lymphocyte count decreased (52%), gamma-glutamyl transferase (GGT) increased (52%), alanine aminotransferase (ALT) increased (44%), hemoglobin decreased (42%), lipase increased (42%), calcium decreased (27%), glucose decreased (26%), and activated partial thromboplastin time (aPTT) prolonged (21%). The most common grade 3/4 laboratory abnormalities (incidence ≥5%) were glucose increased (39%), GGT increased (11%), lymphocyte count decreased (8%), lipase increased (7%), and potassium decreased (6%).

**Please click here for full Prescribing Information.**

FoundationOne®CDx and FoundationOne®Liquid CDx are qualitative next-generation sequencing based in vitro diagnostic tests for advanced cancer patients with solid tumors and are for prescription use only. FoundationOne CDx utilizes FFPE tissue and analyzes 324 genes as well as genomic signatures. FoundationOne Liquid CDx analyzes 324 genes utilizing circulating cell-free DNA and is FDA-approved to report short variants in 311 genes. The tests are companion diagnostics to identify patients who may benefit from treatment with specific therapies in accordance with the therapeutic product labeling. Additional genomic findings may be reported and are not prescriptive or conclusive for labeled use of any specific therapeutic product. Use of the tests does not guarantee a patient will be matched to a treatment. A negative result does not rule out the presence of an alteration. Some patients may require a biopsy for testing with FoundationOne CDx when archival tissue is not available which may pose a risk. Patients who are tested with FoundationOne Liquid CDx and are negative for companion diagnostic mutations should be reflexed to tumor tissue testing and mutation status confirmed using an FDA-approved tumor tissue test, if available. For the complete label, including companion diagnostic indications and important risk information, please visit www.F1CDxLabel.com and www.F1LCDxLabel.com.
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References