Indication
PIQRAY® (alpelisib) tablets 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.
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, retest the patient with tumor tissue.

FDA-approved single-gene tissue and plasma testing for PIK3CA mutation

QIAGEN therascreen® PIK3CA RGQ PCR Kit

therascreen is a registered trademark of QIAGEN group.

See FAQs on page 4
Tumor tissue and plasma testing available

**Tumor tissue**

Mutational testing for PIK3CA may be integrated into MBC workup using archival specimens or recent or new biopsies.\(^2\)*

Decalcified bone metastasis tissue will not be accepted for this test, as it will produce an invalid result.\(^3\)

Assessment may be completed using primary tumor or metastatic sites.\(^2\)

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

**Order online at NeoLINK®† by clicking here**

- Track your order
- Confirm order has been received
- Confirm sample has arrived
- Find results
- NeoGenomics generally expects to provide results within 1 week of specimen receipt

Schedule your specimen pickup by calling Client Services at **1-866-776-5907, option #1.**

**Prefer to use fax?**
Click here to print out the form and fax.

*Existing NeoGenomics Laboratories customer?*
Please include the pathology report and submit by fax to **1-239-690-4237**, or include with patient's specimen in the provided shipper.

*First-time NeoGenomics Laboratories customer?*
Please contact NeoGenomics Laboratories Client Services directly at **1-866-776-5907, option #3** to set up your new customer account before sending in your Request Form.

**Plasma specimen**

If you are interested in ordering a plasma test (PIK3CA mutations can be detected in circulating tumor DNA), you would require local capabilities including access to a 4°C capable centrifuge, -80°C specimen freezer, and dry ice.\(^4\) Please contact NeoGenomics Client Services directly at **1-866-776-5907, option #3** to walk through a prequalification checklist or to view the checklist go to https://neogenomics.com/pik3ca-plasma-prequalification.

Note: If PIK3CA mutations are not detected using plasma, retest the patient using tumor tissue.

\(*This is an external website independently operated and not managed by Novartis Pharmaceuticals Corporation. Novartis assumes no responsibility for the site. NeoLink is a registered trademark of NeoGenomics Laboratories, Inc.*

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**Online ordering at NeoLINK® is the preferred ordering method**

Please see pages 8-9 for Important Safety Information. Please click here for full Prescribing Information.
Frequently asked questions

What sample type is required for the QIAGEN therascreen® PIK3CA RGQ PCR Kit? Can I use primary tumor or metastatic sites? Can I test archival tissue?

For the QIAGEN therascreen® PIK3CA RGQ PCR Kit, primary breast tumor tissue or metastatic tissue specimens may be used, including archival tissue specimens and recent or new biopsies. Tumors not originating in the breast are not accepted for this test.

Plasma derived from peripheral whole blood may also be used for testing. If you are ordering through the PIK3CA CDx Testing Program, please contact NeoGenomics Client Services at 1-866-776-5907, or to learn more about ordering, please visit www.neogenomics.com/pik3ca.

If not, please contact the lab you are ordering the test from.

How long does it take to receive PIK3CA mutation testing results through NeoGenomics?

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

If a PIK3CA mutation is not detected in a plasma specimen, what should I do?

If PIK3CA mutations are not detected using plasma, retest the patient using tumor tissue.

Can I test bone metastases?

NeoGenomics will not accept decalcified bone metastasis tissue for the PIK3CA Mutation CDx test, as it will produce an invalid result.

Which HR/HER2 biomarker profiles qualify?

Participation in the PIK3CA CDx Testing Program is available to patients whose tumors are metastasized, HR+, HER2-, and progressed on or after an endocrine-based regimen.

Have more questions?

Additional FAQs are answered on the NeoGenomics website at www.neogenomics.com/pik3ca and the PIK3CA Testing Navigator website at www.PIK3CA-testing.com.
Questions?
Please call 1-866-776-5907

Ready to order?
Access your NeoLINK® account for immediate access to place orders. Don't have an account? Set one up today by calling 1-866-776-5907, option #3.

Prefer to print this form?
Click here

Remember, this ordering form is for tissue tests only. To order a plasma test, contact NeoGenomics Client Services at 1-866-776-5907, option #1

Please see pages 8-9 for Important Safety Information. Please click here for full Prescribing Information.

NeoLink is a registered trademark of NeoGenomics Laboratories, Inc.

NeoGenomics Laboratories will conduct tumor tissue testing using the QIAGEN therascreen® PIK3CA RGQ PCR Kit. Appropriate patients may receive one tumor tissue 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. 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.

To order a plasma test, contact NeoGenomics Client Services at 1-866-776-5907, option #1.
Key contacts

NeoGenomics Laboratories
Client Services
1-866-776-5907
New account set up, option #3
Specimen pick up, option #1
Plasma prequalification, option #3
PIK3CA Tissue Testing Form
Fax: 1-239-690-4237
neogenomics.com/pik3ca
Order online through NeoLINK® here

Novartis Specialist
hcp.novartis.com/contact

PIQRAY® (alpelisib) tablets
5mg 10mg 200mg

PIQRAY Website
For a general introduction to PIK3CA mutation testing, please visit PIQRAY® (alpelisib) tablets at
HCP-PIQRAY.com/Testing

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

NeoLink is a registered trademark of NeoGenomics Laboratories, Inc.

Please see pages 8-9 for Important Safety Information. Please click here for full Prescribing Information.
PIK3CA Mutation CDx Test Request Form

NeoGenomics Laboratories will conduct tumor tissue testing using the QIAGEN therascreen® PIK3CA RGQ PCR Kit.1 Appropriate patients may receive one tumor tissue 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.

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Physician information

ORDERING PHYSICIAN NAME

PHYSICIAN NPI

ADDRESS

CITY

STATE

ZIP CODE

PHONE #

FAX #

Treating physician

TREATING PHYSICIAN NAME

NPI

Patient information

LAST NAME

FIRST NAME

DATE OF BIRTH (MM/DD/YYYY)

GENDER

Male □ Female □

MRN/PATIENT ID

Specimen/clinical information

COLLECTION DATE (MM/DD/YYYY)

BODY SITE

SPECIMEN TYPE (QUANTITY)

Paraffin Block(s)

Unstained Slides (6-12 slides + H&E)

SPECIMEN ID

LOCATION OF SPECIMEN

ADDRESS

CITY

STATE

ZIP CODE

PHONE #

FAX #

I certify that I am the health care professional who has ordered the above mutation testing for the identified patient, who has consented to the mutation testing, that I have made an independent judgment that the above testing is medically necessary, within the FDA-approved prescribing information and that the information provided is accurate to the best of my knowledge.

AUTHORIZED SIGNATURE

DATE (MM/DD/YYYY)

Questions?

Please call 1-866-776-5907

To order a plasma test, contact NeoGenomics Client Services at 1-866-776-5907, option #1.

Existing NeoGenomics customers

Please include the pathology report and submit by fax to 1-239-690-4237, or include with patient specimen in the provided shipper.

First time ordering with NeoGenomics?

Please fax this form and pathology report to 1-239-690-4237 so we can set up your account prior to receiving the specimen. A Client Services representative will contact you to assist you with your first order.

therascreen® is a registered trademark of QIAGEN group.

Please see indication and Important Safety Information for alpelisib on next page or click here for full Prescribing Information.
Important Safety Information

Indication
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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.

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
Important Safety Information (cont)

treatment. Closely monitor patients with diabetes.

**Hyperglycemia (cont):** 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).

**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%).