

Patient leaflet in accordance with the Pharmacists’ Regulations (Preparations) - 1986

This medicine is dispensed with a doctor’s prescription only

PIQRAY 50 mg

PIQRAY 150 mg

PIQRAY 200 mg

Film-coated tablets

Each film-coated tablet contains:

PIQRAY 50 mg: apelisib 50 mg

PIQRAY 150 mg: apelisib 150 mg

PIQRAY 200 mg: apelisib 200 mg

Inactive ingredients and allergens: See section 2 under 'Important information about some of this medicine’s ingredients' and section 6 ‘Additional information’.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

1.What is this medicine intended for?

PIQRAY in combination with fulvestrant is intended for 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 following progression on or after an endocrine-based treatment regimen.

Your doctor will test your cancer for an abnormal “PIK3CA” gene to make sure that treatment with PIQRAY is right for you.

Therapeutic group: phosphatidylinositol-3-kinase (PI3K) inhibitor.

2.Before using this medicine

Do not use this medicine if:

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| <ul style="list-style-type: none">You are sensitive (allergic) to the active ingredient apelisib or to any of the other ingredients in this medicine. For a list of inactive ingredients, see section 6 ‘Additional information’. |
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Special warnings about using this medicine

Before treatment with PIQRAY, tell your doctor if:

- you have a history of diabetes.
- you have a history of skin rash, redness of skin, blistering of the lips, eyes or mouth or skin peeling.
- you are pregnant, plan to become pregnant, or are breast-feeding (also see below under ‘Pregnancy, breast-feeding, and fertility’).
- you are **male** and have a female partner who is able to become pregnant (also see below under ‘Pregnancy, breast-feeding, and fertility’).

Tell your doctor or get immediate medical help if any of the following conditions apply to you during treatment with PIQRAY:

- you have trouble breathing, swelling of the face or throat, flushing, rash, fever or fast heart rate during treatment with PIQRAY (possible signs of severe allergic reactions).
- you get severe rash or rash that keeps getting worse, reddened skin, flu-like symptoms, blistering of the lips, eyes or mouth, blisters on the skin or skin peeling, with or without fever (possible signs of severe skin reactions).

Tell your doctor immediately, if:

- you develop symptoms of hyperglycemia, including excessive thirst, dry mouth, more frequent urination than usual or a higher amount of urine than normal, increased appetite with weight loss, confusion, nausea, vomiting, fruity odor from the mouth, difficulty breathing, dry or flushed skin.

- you develop new or worsening symptoms of lung problems, including shortness of breath or trouble breathing, cough, chest pain (possible signs of pneumonitis).

- you develop diarrhea, stomach-area (abdominal) pain, or see mucus or blood in your stool (possible signs of colitis) during treatment with PIQRAY. Your doctor may tell you to drink more fluids or take medicines to treat diarrhea or colitis.

Other medicines and PIQRAY

If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist.

PIQRAY and other medicines may affect each other causing side effects.

- **Cytochrome CYP3A4 inducers:**

Coadministration of PIQRAY with strong cytochrome CYP3A4 inducers may decrease the concentration of apelisib in your blood. This may reduce the activity of the active ingredient apelisib. Avoid taking PIQRAY with strong cytochrome CYP3A4 inducers (e.g., rifampicin).

- **Breast Cancer Resistance Protein (BCRP) Inhibitors**

Coadministration of PIQRAY with a BCRP inhibitor may increase apelisib concentration, which may increase the risk of toxicity. Avoid taking BCRP inhibitors during treatment with PIQRAY. If you are unable to use alternative medicines, when PIQRAY is given in combination with BCRP inhibitors, your doctor will closely monitor you for increased side effects.

- **Cytochrome CYP2C9 substrates**

Coadministration of PIQRAY with cytochrome CYP2C9 substrates (such as warfarin), may decrease the concentration of these medicines in your plasma. Your doctor will monitor you closely when PIQRAY is given in combination with cytochrome CYP2C9 substrates, because a decrease in plasma concentration of cytochrome CYP2C9 substrates may decrease the activity of these medicines.

Know the medicines you take. Keep a list of them to show your doctor or pharmacist when you get a new medicine.

Children and adolescents

Piqray is not intended for use in children and adolescents under 18 years old.

Using this medicine and food

Take PIQRAY with food.

Tests and follow-up

Your doctor will carry out blood tests to monitor your blood sugar before and during treatment with PIQRAY.

Based on the results, your doctor will decide whether to temporarily stop your treatment with PIQRAY, reduce your dosage, or discontinue your treatment.

Pregnancy, breast-feeding, and fertility

Pregnancy

If you are pregnant, think you are pregnant, or plan to become pregnant consult your doctor before starting treatment with PIQRAY.

PIQRAY can harm your unborn baby.

If you are a female who is able to become pregnant, your doctor will check to see if you are pregnant before you start treatment with PIQRAY.

You should use effective contraception during treatment with PIQRAY and for one week after the last dose. Talk to your doctor about birth control methods that may be right for you during this time.

If, during treatment with PIQRAY, you become pregnant or think you are pregnant, tell your doctor right away.

Males with female partners who are able to become pregnant, should use condoms and effective contraception during treatment with PIQRAY and for one week after the last dose. If your female partner becomes pregnant, tell your doctor right away.

Breast-feeding

Do not breastfeed during treatment with PIQRAY and for one week after the last dose. It is not known if PIQRAY passes into breast milk.

Fertility

PIQRAY may affect fertility in males and in females who are able to become pregnant. Talk to your doctor if this is a concern for you.

PIQRAY is coadministered with fulvestrant. You should also read the fulvestrant patient information leaflet for important pregnancy, birth control, breast-feeding, and fertility information.

Driving and using machines

Treatment with PIQRAY may lead to tiredness. Therefore, while you are taking PIQRAY, you should be cautious when driving or using machines.

Important information about some of this medicine’s ingredients

This medicine contains less than 1 mmol sodium (23 mg) per film-coated tablet, which means it is essentially ‘sodium-free’.

3.How to use this medicine?

Always use this medicine according to your doctor’s instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine. Only your doctor will determine your dose and how you should take this medicine.

The recommended dosage is usually 300 mg (two 150 mg tablets) taken orally, once a day.

If you vomit after taking a dose of PIQRAY, do not take another dose on that day. Take your next dose at your usual time.

Your doctor will determine the dose of fulvestrant you should receive and when you should receive it.

Depending on how your body responds to treatment with PIQRAY, your doctor may want to adjust your PIQRAY dose.

Do not change your dose unless your doctor tells you.

Do not exceed the recommended dose.

• **Treatment duration**

Do not stop taking PIQRAY unless your doctor tells you.

• **How to take PIQRAY**

- Take PIQRAY one time each day, at about the same time each day.
- Take PIQRAY with food.
- Swallow PIQRAY tablets whole. Do not chew, crush, or split the tablets.
- Do not take any PIQRAY tablets that are broken, cracked, or that look damaged.

If you have accidentally taken a higher dose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

If you forget to take the medicine at the scheduled time, you may still take it with food up to 9 hours after the time you usually take it. If it has been more than 9 hours after you usually take your dose, skip the dose for that day. The next day, take the dose at your usual time. Do not take 2 doses to make up for a missed dose.

Adhere to the treatment as recommended by your doctor.

Even if your health improves, do not stop taking this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and dose each time you take medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4.Side effects

Like with all medicines, using PIQRAY may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

If you experience any of the following serious side effects, contact your doctor right away.

Your doctor may tell you to decrease your dose, temporarily stop your treatment, or completely stop your treatment with PIQRAY if you get certain serious side effects.

PIQRAY may cause serious side effects, including:

• **Severe allergic reactions.** Tell your doctor or get immediate medical help if you have trouble breathing, swelling of the face or throat, flushing, rash, fever, or fast heart rate during treatment with PIQRAY.

• **Severe skin reactions.** Tell your doctor or get immediate medical help if you get severe rash or rash that keeps getting worse, reddened skin, flu-like symptoms, blistering of the lips, eyes or mouth, blisters on the skin or skin peeling, with or without fever.

• **High blood sugar levels (hyperglycemia).** Hyperglycemia is common with PIQRAY and can be severe. Your doctor will monitor your blood sugar levels before you start and during treatment with PIQRAY. Your doctor may monitor your blood sugar levels more often if you have a history of type 2 diabetes. Tell your doctor right away if you develop symptoms of hyperglycemia including:

- excessive thirst
- dry mouth
- more frequent urination than usual or a higher amount of urine than normal
- increased appetite with weight loss
- confusion
- nausea
- vomiting
- fruity odor from the mouth
- difficulty breathing
- dry or flushed skin

• **Lung problems (pneumonitis - inflammation of the lung tissue).** Tell your doctor right away if you develop new or worsening symptoms of lung problems, including:

- shortness of breath or trouble breathing
- cough
- chest pain.

• **Diarrhea or colitis (inflammation of your intestines).** Diarrhea is common with PIQRAY and can be severe. Severe diarrhea can lead to the loss of too much body water (dehydration) and kidney injury. If you develop diarrhea, stomach-area (abdominal) pain, or see mucus or blood in your stool during treatment with PIQRAY, tell your doctor right away. Your doctor may tell you to drink more fluids or take medicines to treat diarrhea or colitis.

Other serious and common side effects of using PIQRAY with fulvestrant include:

- acute kidney damage
- abdominal pain
- anemia
- osteonecrosis of the jaw.

Additional side effects:

Very common side effects (may affect more than one in 10 users):

- rash
- nausea
- tiredness and weakness
- decreased appetite
- vomiting
- weight loss
- hair loss
- stomatitis (inflammation of the oral mucosa, including mouth sores, aphthous ulcer and mouth ulceration)
- indigestion
- mucosal inflammation
- peripheral edema
- pyrexia (high fever)
- mucosal dryness (including dry mouth, dry vagina and vulva)
- disorders in sense of taste (dysgeusia) (including loss of sense of taste and reduced sensitivity to flavors)
- headache
- itching (pruritus)
- dry skin
- abdominal pain
- changes in certain blood tests:
 - high blood levels of the following enzymes: gamma-glutamyltransferase, alanine aminotransferase, lipase
 - high level of creatinine in the blood
 - low blood levels of lymphocytes, platelets, glucose, hemaglobin and/or albumin
 - activated partial thromboplastin time prolonged (a measure of blood clotting function)
 - decreased level of calcium in the blood
 - decreased level of potassium in the blood
 - decreased level of magnesium in the blood.

Common side effects (may affect 1-10 in 100 users):

- urinary tract infection.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link ‘Reporting Side Effects of Drug Treatment’ on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: <https://sideeffects.health.gov.il>

5.How to store the medicine?

Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.

Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.

Storage conditions: Do not store above 30°C. Protect from moisture.

6.Additional information

In addition to the active ingredient, this medicine also contains:

Tablet core:

microcrystalline cellulose, mannitol, sodium starch glycolate, hypromellose, magnesium stearate

Coating material:

hypromellose, iron oxide black, iron oxide red, titanium dioxide, macrogol 4000, talc

What the medicine looks like and contents of the pack:

PIQRAY 50 mg film-coated tablets are light pink, round tablets, imprinted with “L7” on one side and “NVR” on the other side.

PIQRAY 150 mg film-coated tablets are pale red, oval tablets, imprinted with “UL7” on one side and “NVR” on the other side.

PIQRAY 200 mg film-coated tablets are light red, oval tablets, imprinted with “YL7” on one side and “NVR” on the other side.

PIQRAY is supplied as film-coated tablets in blister trays. PIQRAY is available in the following pack sizes:

- Combination packs containing 50 mg and 200 mg film-coated tablets (for patients taking 250 mg daily dose):
 - Packs containing a 28-day supply: 56 film-coated tablets (28 of 50 mg and 28 of 200 mg).
- Packs containing 150 mg film-coated tablets (for patients taking 300 mg daily dose):
 - Packs containing a 28-day supply: 56 film-coated tablets.

- Packs containing 200 mg film-coated tablets (for patients taking 200 mg daily dose):
 - Packs containing a 28-day supply: 28 film-coated tablets.

Not all pack sizes may be marketed.

Registration holder and importer’s name and address: Novartis Israel Ltd., P.O.B 7126, Tel Aviv.

Registration number of the medicine in the Ministry of Health’s National Drug Registry:

PIQRAY 50 mg: 166-20-36150

PIQRAY 150 mg: 166-18-36148

PIQRAY 200 mg: 166-19-36149

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