Package leaflet: Information for the patient

Piqray® 50 mg film-coated tablets
Piqray® 150 mg film-coated tablets
Piqray® 200 mg film-coated tablets
alpelisib

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, or pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Piqray is and what it is used for
2. What you need to know before you take Piqray
3. How to take Piqray
4. Possible side effects
5. How to store Piqray
6. Contents of the pack and other information

1. What Piqray is and what it is used for

What Piqray is
Piqray contains the active substance alpelisib, which belongs to a group of medicines called phosphatidylinositol-3-kinase (PI3K) inhibitors.

What Piqray is used for
Piqray is used for the treatment of postmenopausal women, and men, with a type of breast cancer called advanced hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer. Piqray is used in combination with fulvestrant, a hormonal anticancer therapy, in patients whose cancer has not responded to other hormonal treatments and who have certain changes (mutations) in a gene called PIK3CA.

Your doctor will take a sample of your blood and/or tumour tissue, which will be tested for these PIK3CA mutations. If the result is positive your cancer is likely to respond to treatment with Piqray.

How Piqray works
Piqray works by blocking the effects of enzymes called phosphatidylinositol-3-kinases (PI3K). These enzymes help cancer cells to grow and multiply. By blocking their action, Piqray can reduce growth and spread of the cancer and help to destroy cancer cells.

If you have any questions about how Piqray works or why this medicine has been prescribed for you, ask your doctor, pharmacist or nurse.

2. What you need to know before you take Piqray

Follow all of your doctor's instructions carefully, as they may differ from the general information in this leaflet. Check with your doctor if you are not sure.

Do not take Piqray
- if you are allergic to alpelisib or any of the other ingredients of this medicine (listed in section 6). If you think you may be allergic, ask your doctor for advice.

Warnings and precautions
Talk to your doctor or pharmacist before taking Piqray.

If any of the following apply to you before taking Piqray, tell your doctor or pharmacist:
- if you have or have ever had high levels of sugar in your blood or diabetes (or signs of increased sugar levels, such as excessive thirst and dry mouth, needing to pass urine more often than usual, producing greater amounts of urine than usual, tiredness, nausea, increased appetite with weight loss).
- if you have ever had Stevens-Johnson syndrome (SJS, a highly serious reaction with flu-like symptoms and painful rash affecting the skin, mouth, eyes and genitals), erythema multiforme (EM, a skin reaction that causes red spots or patches on the skin, that may look like a target or "bullseye" with a dark red centre surrounded by paler red rings), drug reaction with eosinophilia and systemic symptoms (DRESS, a skin reaction combined with fever, facial swelling, enlarged lymph nodes and kidney or liver injury) or toxic epidermal necrolysis (TEN, a serious skin reaction with red skin, blistering of the lips, eyes or mouth, skin peeling, with or without fever, rash).
- if you have a severe bone disease that affects the jaw (osteonecrosis of the jaw, ONJ).

If any of the following apply to you during your treatment with Piqray, tell your doctor or pharmacist immediately:
- Rash, itching, hives, breathlessness, difficulty breathing, wheezing, cough, light-headedness, dizziness, changes in levels of consciousness, low blood pressure, reddening of the skin, swelling of the face or throat, blue discoloration of the lips, tongue or skin (possible signs of severe allergic reactions).
- New or changing breathing problems such as difficult or painful breathing, cough, rapid breathing, blue discoloration of the lips, tongue or skin, hiccups (possible signs of non-infectious pneumonitis or pneumonia).
- Increased thirst and dry mouth, passing urine more often than usual, tiredness, increased appetite with weight loss, confusion, nausea, vomiting, fruity odour on breath, difficulty breathing and dry or flushed skin, which may be signs of increased blood sugar levels (hyperglycaemia) and its complications.
- Rash, reddening of the skin, blistering of the lips, eyes or mouth, skin peeling, sometimes with fever (possible signs of one of the following skin conditions: Stevens-Johnson syndrome (SJS), erythema multiforme (EM), drug reaction with eosinophilia and systemic symptoms (DRESS) or toxic epidermal necrolysis (TEN)).
- New or worsening symptoms affecting your mouth (such as loose teeth, pain or swelling, non-healing of mouth sores, or discharge).
- Severe diarrhoea or severe abdominal pain or stools with mucus or blood, which may be signs of inflammation of your intestine (colitis).

Your doctor may need to treat these symptoms, temporarily interrupt your treatment, reduce your dose, or permanently stop your treatment with Piqray.

Blood tests before and during your treatment with Piqray
Your doctor will carry out blood tests before and regularly during treatment with Piqray to monitor your blood sugar. Based on the results, your doctor will take any necessary actions, such as prescribing a medicine to lower blood sugar levels. If necessary, your doctor may decide to temporarily interrupt treatment with Piqray or reduce your Piqray dose to allow your blood sugar to decrease. Your doctor may also decide to stop Piqray treatment permanently.

Make sure that you regularly test your blood sugar before you start treatment, during treatment and after you stop treatment with Piqray.
- Your doctor will tell you exactly when and where to have the blood tests. Treatment with Piqray may only be started if tests show that you have the right levels of sugar in your blood. This is

because Piqray can increase sugar in your blood (hyperglycaemia), which could be serious and need treatment. Only regular fasting blood tests can tell the doctor if you are developing hyperglycaemia.
- Your doctor will tell you exactly when and where to test your blood sugar. This will be required more frequently in the first 4 weeks of treatment and especially in the first 2 weeks of treatment with Piqray. Afterwards, blood tests will be needed at least once a month, depending on your blood sugar levels.

Children and adolescents
Piqray is not to be used in children and adolescents under 18 years of age.

Other medicines and Piqray
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes in particular:
- eltrombopag, a medicine used to treat low platelet count
- medicines used to treat breast cancer (such as lapatinib, ribociclib)
- everolimus, apalutamide, enzalutamide and mitotane, medicines used to treat certain types of cancers
- pantoprazole, a medicine used to treat heartburn and reduce the amount of acid produced in your stomach
- midazolam, a medicine used to for sedation or sleep disturbances
- rifampicin, a medicine to treat tuberculosis and some other serious infections
- carbamazepine and phenytoin, medicines used to treat seizures or convulsions
- St. John's Wort, a herbal product used to treat depression and other conditions
- encorafenib, a medicine used to treat a certain type of skin cancer
- warfarin, a medicine used reduce the clotting ability of the blood

Ask your doctor or pharmacist if you are not sure whether your medicine is one of the medicines listed above.

Pregnancy, breast-feeding and fertility
Piqray must not be used by women who are, or may be pregnant or breast-feeding. Piqray may harm an unborn baby. If you think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. Women should not breast-feed during treatment and for at least 1 week after the last dose of Piqray. Your doctor will discuss with you the potential risks of taking Piqray during pregnancy or breast-feeding.

If you are a woman who could become pregnant, your doctor will rule out an existing pregnancy before starting you on treatment with Piqray. This may include having a pregnancy test.

Women who could become pregnant should use an effective method of birth control during treatment and for at least 1 week after stopping Piqray. Ask your doctor about suitable methods. If you think you may be pregnant after starting treatment with Piqray, tell your doctor immediately.

During treatment and for at least 1 week after stopping treatment, male patients should use a condom for intercourse with female partners who could become pregnant. If the partner of a male patient suspects that she has become pregnant during this time, she should inform a doctor immediately.

Driving and using machines
Treatment with Piqray may lead to tiredness or blurred vision. You should therefore be cautious when driving or using machines during your treatment with Piqray.

Piqray contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per film-coated tablet, that is to say essentially 'sodium-free'.

3. How to take Piqray

Always take this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

How much Piqray to take
The usual starting dose of Piqray is 300 mg once daily. Your doctor will decide on the right dose for you.

Depending on the dose prescribed, the number of tablets to take is as follows:
- 300 mg dose: two 150 mg tablets
- 250 mg dose: one 200 mg tablet and one 50 mg tablet
- 200 mg dose: one 200 mg tablet

Depending on how your body responds to the treatment with Piqray, your doctor may want to adjust your Piqray dose. It is very important to follow your doctor's instructions. If you have certain side effects, your doctor may ask you to change to a lower dose, to interrupt treatment for a time, or to stop treatment.

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

When to take Piqray
Piqray tablets are supplied in packs containing blister cards. Each blister card shows the tablet(s) to be taken on each day of the week. Follow the instructions on the blister card.

Take Piqray once a day, immediately after food. Taking Piqray at the same time each day will help you to remember when to take your medicine.

How to take Piqray
Piqray tablets should be swallowed whole, they should not be chewed, crushed or split before swallowing. You should not swallow any tablet that is broken, cracked or otherwise damaged as you may not be taking the full dose.

If you vomit after you take the Piqray tablet(s), do not take any more tablets until your next scheduled dose.

How long to take Piqray
Take Piqray for as long as your doctor tells you to.

This is a long-term treatment, possibly lasting for months or years. Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.

If you have questions about how long to take Piqray, talk to your doctor or to your pharmacist.

If you take more Piqray than you should
People who have taken too many Piqray tablets have experienced effects that are known side effects of Piqray, including high blood sugar levels, nausea, tiredness and rash. If you accidentally take too many tablets, or if someone else accidentally takes your medicine, contact a doctor or hospital for advice immediately. Medical treatment may be necessary.

If you forget to take Piqray
If you forget to take a dose of Piqray, you may still take it, immediately after food, up to 9 hours after the time you should have taken it. If you only remember more than 9 hours after you should have taken it, skip the dose for that day. The next day, take the dose at your usual time. Do not take a double dose to make up for the one that you missed.

If you stop taking Piqray
Stopping your treatment with Piqray may cause your condition to become worse. Do not stop taking Piqray unless your doctor tells you to stop.

If you have any further questions on the use of Piqray, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Some side effects could be serious
If you get any serious side effects, **stop taking this medicine and tell your doctor immediately**.

Very common (*may affect more than 1 in 10 people):*
- Feeling very thirsty, passing urine more often than usual or passing greater amounts of urine than usual, increased appetite with weight loss (possible symptoms of high blood sugar levels, also called hyperglycaemia)
- Fever, cough, runny nose, enlarged lymph nodes, painful joints, rash, night sweats, weight loss (possible symptoms of a low level of lymphocytes, a type of white blood cells)

Common (*may affect up to 1 in every 10 people):*
- Rash, itching, hives, breathlessness, difficulty breathing, wheezing, cough, light-headedness, dizziness, changes in levels of consciousness, low blood pressure, reddening of the skin, swelling of the face and/or throat, blue discoloration of the lips, tongue or skin (possible signs of severe allergic reactions)
- Difficulty breathing, headache, nausea, vomiting (possible symptoms of a condition called ketoacidosis that involves a high level of acids in the blood)
- Breathing problems including difficult or painful breathing, cough, rapid breathing, blue discoloration of the lips, tongue or skin, hiccups (possible symptoms of pneumonitis)
- Passing urine less often than usual or passing smaller amounts of urine than usual, swelling in legs, ankles and around the eyes, tiredness, confusion, nausea, seizure, chest pain (possible symptoms of acute kidney failure)
- Pain, swelling or numbness of the jaw, a feeling of heaviness in the jaw or loosening of a tooth (possible symptoms of osteonecrosis of the jaw)
- Rash, skin reddening, blistering of lips, eyes or mouth, skin peeling (possible symptoms of erythema multiforme)

Uncommon (*may affect up to 1 in every 100 people):*
- Severe upper stomach pain (possible symptoms of pancreatitis)
- Rash, red skin, blistering of the lips, eyes or mouth, skin peeling, fever (possible symptoms of Stevens-Johnson syndrome)

Not known (*frequency cannot be estimated from the available data):*
- Diarrhoea, an increased number of bowel movements than usual, blood in your stools or darker-coloured stools, pain or tenderness in your stomach area (possible symptoms of colitis, inflammation of the intestines).
- Confusion, dry mouth, dry or flushed skin, nausea, vomiting, tiredness, need to pass urine frequently, thirst (possible symptoms of hyperglycaemic hyperosmolar nonketotic syndrome (HHNKS))
- Swelling of your face or throat and difficulty breathing (possible symptoms of angioedema, a type of severe allergic reaction).
- Rash, fever (possible symptoms of drug rash with eosinophilia and systemic symptoms (DRESS))
- Redness of the eye, eye pain, sensitivity to light, dark floaters in your field of vision, blurred vision, decrease in vision, small pupil (possible symptoms of uveitis)

Other possible side effects
Other side effects include the following listed below. If these side effects become severe, tell your doctor, pharmacist or nurse.

Very common (*may affect more than 1 in 10 people):*
- Painful and frequent urination (possible symptoms of urinary tract infection)
- Tiredness, pale skin (possible symptoms of anaemia, a condition involving a low level of red blood cells)
- Spontaneous bleeding or bruising (signs of a low level of thrombocytes, also called platelets, in the blood)
- Loss of appetite
- Headache
- Strange taste in the mouth (dysgeusia)
- Diarrhoea
- Nausea
- Vomiting
- Mouth sores or ulcers with gum inflammation (stomatitis)
- Abdominal pain
- Upset stomach, indigestion (dyspepsia)
- Rash
- Hair loss or hair thinning (alopecia)
- Itching (pruritus)
- Dry skin
- Tiredness (fatigue)
- Pain, redness and swelling of airways or food pipe or genital mucosa (mucosal inflammation)
- Swollen hands, ankles or feet (peripheral oedema)
- Fever (pyrexia)
- Mucosal dryness
- Weight decreased
- Reduced level of calcium in the blood, which may sometimes lead to cramps (hypocalcaemia)
- Reduced level of potassium in the blood, associated with muscle weakness, muscle spasms and/or abnormal heart rhythm (hypokalaemia)
- Headache, dizziness (possible symptoms of high blood pressure)

Common (*may affect up to 1 in every 10 people)*:
- Dehydration
- Problems falling asleep (insomnia)
- Dry eye
- Blurred vision
- Swelling of part or all of your arm (including fingers) or leg (including toes), feeling of heaviness, restricted movement, discomfort, thickening of the skin and recurring infections (possible symptoms of lymphoedema)
- Toothache
- Bleeding, tender or enlarged gums (signs of inflammation of the gums)
- Cracked, chapped lips (cheilitis)
- Gingival pain
- Erythema
- Skin inflammation with rash (dermatitis)
- Reddening and/or swelling and possibly peeling on the palms of the hands and soles of the feet, which may be accompanied by a tingling sensation and burning pain (signs of hand-foot syndrome)
- Muscle spasms
- Muscle pain (myalgia)
- Generalised swelling (oedema)

During Piqray treatment, the results of some blood tests may be abnormal, as follows:

Very common (*may affect more than 1 in 10 people)*:
- High blood levels of the following enzymes: gamma glutamyl transferase, alanine aminotransferase, lipase
- High blood level of sugar
- High blood level of creatinine and/or calcium
- Low blood level of lymphocytes, platelets, sugar, haemoglobin and/or albumin
- Increase in activated partial thromboplastin time (a measurement of blood clotting ability)

Common (*may affect up to 1 in every 10 people)*:
- High blood level of glycosylated haemoglobin (a marker of blood sugar level over the last 8 to 12 weeks)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Piqray

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and the blister card after "EXP". The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

Do not take this medicine if you notice any damage to the packaging or if there are any signs of tampering.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Piqray contains
- The active substance of Piqray is alpelisib.
- Each 50 mg Piqray film-coated tablet contains 50 mg alpelisib.
- Each 150 mg Piqray film-coated tablet contains 150 mg alpelisib.
- Each 200 mg Piqray film-coated tablet contains 200 mg alpelisib.
- The other ingredients are:
  - Tablet core: cellulose microcristalline, mannitol, sodium starch glycolate (see section 2 "Piqray contains sodium"), hypromellose, magnesium stearate.
  - Coating material: Hypromellose, iron oxide red and black (E172), titanium dioxide (E171), macrogol, talc.

What Piqray 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. Approximate diameter: 7.2 mm.

Piqray 150 mg film-coated tablets are pale red, ovaloid tablets, imprinted with "UL7" on one side and "NVR" on the other side. Approximate size: 14.2 mm (length); 5.7 mm (width).

Piqray 200 mg film-coated tablets are light red, ovaloid tablets, imprinted with “YL7” on one side and “NVR” on the other side. Approximate size: 16.2 mm (length); 6.5 mm (width).

Piqray is supplied as film-coated tablets in blisters. Piqray is available in the following pack sizes:
- Packs containing 50 mg and 200 mg film-coated tablets (for patients on 250 mg daily dose):
  - Packs containing 14-day supply: 28 film-coated tablets (14 of 50 mg and 14 of 200 mg).
  - Packs containing 28-day supply: 56 film-coated tablets (28 of 50 mg and 28 of 200 mg).
  - Multipacks containing 168 film-coated tablets (3x 56, each comprising 28 tablets of 50 mg and 28 tablets of 200 mg).
- Packs containing 150 mg film-coated tablets (for patients on 300 mg daily dose)
  - Packs containing 14-day supply: 28 film-coated tablets.
  - Packs containing 28-day supply: 56 film-coated tablets.
  - Multipacks containing 168 (3x 56) film-coated tablets.
- Packs containing 200 mg film-coated tablets (for patients on 200 mg daily dose)
  - Packs containing 14-day supply: 14 film-coated tablets.
  - Packs containing 28-day supply: 28 film-coated tablets.
  - Multipacks containing 84 (3x 28) film-coated tablets.

Not all pack sizes may be marketed.

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