PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

Kisqali® 200 mg

Film-coated tablets

Active ingredient:
Each tablet contains: ribociclib 200 mg (as ribociclib succinate 254.40 mg)

Inactive and allergenic ingredients: see section 2 under "Important information about some of the ingredients of the medicine" and section 6 "Further information".

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Kisqali is intended for the treatment in combination with:
- A non-steroidal aromatase inhibitor in pre/perimenopausal or postmenopausal women, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer, as initial endocrine-based therapy.
- Fulvestrant in men and postmenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer, as initial endocrine-based therapy or following disease progression on endocrine therapy.

Therapeutic group: Cyclin-dependent kinase enzyme inhibitors.

Kisqali contains the active ingredient ribociclib, which belongs to a group of medicines called cyclin-dependent kinase (CDK) inhibitors.
Kisqali works by blocking proteins called cyclin-dependent kinases 4 and 6, which are important for the growth and division of cells. Blocking these proteins can slow down the growth of cancer cells and delay the progression of the cancer.

If you have questions about how Kisqali works or why it was prescribed, ask your doctor.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient ribociclib, to peanuts, soya or to any of the additional ingredients in the medicine (see section 6 "Further information").

If you think you may be sensitive, consult your doctor.

Special warnings regarding use of the medicine
Talk to your doctor, pharmacist or nurse before taking Kisqali.

Before treatment with Kisqali, tell the doctor or pharmacist if:
- You have a fever, sore throat or mouth ulcers due to infections (signs of a low level of white blood cells).
- You have liver problems or have previously had any type of liver disease.
- You have or have had heart disorders or heart rhythm disorders, such as irregular heartbeats, including a condition called QT interval prolongation syndrome, or low levels of potassium, magnesium, calcium or phosphorus in the blood.
- You have suffered in the past from excessive blood coagulation or you have known risk factors for excessive blood coagulation.

During treatment with Kisqali, tell your doctor or pharmacist if any of the following apply to you:
- You have a combination of any of the following symptoms: rash, red skin, blistering of the lips, eyes or mouth, skin peeling, high fever, flu-like symptoms and enlarged lymph nodes (signs of a severe skin reaction).
  In case of a severe skin reaction, the doctor will ask you to stop Kisqali treatment immediately.
- You experience breathing problems, coughing and shortness of breath (may be signs of lung or breathing problems).
  If necessary, your doctor may prescribe a lower dose, interrupt Kisqali treatment, or stop it permanently.

Children and adolescents
Kisqali is not intended for treatment of children and adolescents under the age of 18.

Tests and follow-up
The doctor will instruct you to perform regular blood tests before and during treatment with Kisqali to monitor liver function, the levels of blood cells (white blood cells, red blood cells and platelets) and electrolytes (blood salts, including potassium, calcium, magnesium and phosphate) in your body. Your heart activity will also be checked before and during treatment with Kisqali with a test called an electrocardiogram (ECG). If necessary, additional tests to evaluate your kidney function will be performed during treatment with Kisqali. In addition, the doctor may reduce the dosage of Kisqali or temporarily stop treatment, if necessary, to allow the liver, kidney, blood cells, electrolyte levels or heart activity to recover. The doctor may also decide to stop treatment with Kisqali permanently.

Drug interactions
Before you start taking Kisqali, tell the doctor or pharmacist if you are taking, have recently taken or might take other medicines, including non-prescription medicines and nutritional supplements, because they may influence the effect of Kisqali. In particular, if you are taking:
- Tamoxifen, another medicine for the treatment of breast cancer.
- Certain medicines used to treat fungal infections, such as ketoconazole, itraconazole, voriconazole or posaconazole.
- Certain medicines used to treat human immunodeficiency virus (HIV/AIDS), such as ritonavir, saquinavir, indinavir, lopinavir, nelfinavir, telaprevir and efavirenz.
- Certain medicines used to treat seizures (antiepileptics), such as carbamazepine and phenytoin.
- St. John's Wort (also known as *Hypericum perforatum*) - a herbal medicine used to treat depression and other conditions.
- Certain medicines used to treat heart rhythm disorders or high blood pressure, such as amiodarone, disopyramide, procainamide, quinidine, sotalol and verapamil.
- Medicines to treat malaria, such as chloroquine.
- Antibiotics, such as clarithromycin, telithromycin, moxifloxacin, rifampicin, ciprofloxacin, levofloxacin and azithromycin.
- Certain medicines used for sedation or anesthesia, such as midazolam.
- Certain medicines used to treat psychotic problems, such as haloperidol or for psychiatric problems, such as nefazodone.
- Medicines used to treat angina, such as bepridil.
- Methadone, used to treat pain or addiction to opioids.
- Medicines like intravenous ondansetron, used to prevent nausea and vomiting caused by chemotherapy (treatment with cancer medicines).

Kisqali may increase or decrease the blood levels of other medicines. This includes, in particular:
- Medicines used to treat symptoms of benign prostatic hyperplasia, such as alfuzosin.
- Tamoxifen, another medicine used for the treatment of breast cancer.
- Antiarrhythmics, such as amiodarone or quinidine.
- Medicines to treat psychotic problems, such as pimozide or quetiapine.
- Medicines used to improve blood fat levels, such as simvastatin, lovastatin, pitavastatin, pravastatin or rosuvastatin.
- Medicines used to treat high blood sugar levels (e.g. diabetes), such as metformin.
- Medicines used to treat cardiac problems, such as digoxin.
- Medicines used to treat pulmonary arterial hypertension and erectile problems (impotence), such as sildenafil.
- Medicines used to treat low blood pressure or migraine, such as ergotamine or dihydroergotamine.
- Certain medicines used to treat epileptic fits or which are used for sedation, or anesthesia, such as midazolam.
- Medicines used to treat sleep disorders, such as triazolam.
- Analgesics, such as alfentanil and fentanyl.
- Medicines used to treat gastrointestinal problems, such as cisapride.
- Medicines used to prevent the rejection of an organ transplant, such as tacrolimus, sirolimus and ciclosporin (which is also used to treat rheumatoid arthritis and psoriasis).
- Everolimus, used to treat several types of cancer and tuberous sclerosis (also used to prevent the rejection of an organ transplant).

Make sure to tell the doctor about all medicines and food supplements, including herbal medicines, that you are taking before starting treatment with Kisqali and if you have been prescribed a new medicine after starting treatment with Kisqali.

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

Use of the medicine and food
Do not eat grapefruits or drink grapefruit juice during treatment with Kisqali. These may change the way Kisqali is processed in your body and may increase the amount of Kisqali in the bloodstream.
Kisqali can be taken with or without food.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to become pregnant, consult the doctor before taking this medicine.
The doctor will discuss with you the potential risks of taking Kisqali during pregnancy.

Pregnancy and women of childbearing potential
Do not use Kisqali during pregnancy since it may harm your unborn baby. If you are a woman of childbearing potential, you should have a negative pregnancy test before starting treatment with Kisqali. You should use effective contraception (e.g. double-barrier contraception such as a condom and a diaphragm) while taking Kisqali and for at least 21 days after the last dose. Ask the doctor about options for effective contraception.

Breast-feeding
Do not breast-feed while taking Kisqali and for at least 21 days after the last dose.

Driving and using machines
Treatment with Kisqali may cause tiredness, dizziness or a spinning sensation. Therefore, you should be cautious when driving or using machines during treatment with Kisqali.

Important information about some of the ingredients of the medicine
Kisqali contains soya lecithin (0.344 mg per tablet).
Do not use this medicine if you are allergic to peanuts or soya.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use this preparation according to the doctor's instructions.
Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the medicine. Do not change the Kisqali dose or schedule without talking to the doctor.
The dosage and treatment regimen will be determined by the doctor only. The usual dosage is generally:
- The recommended starting dosage of Kisqali is 600 mg (3 tablets of 200 mg), once daily. The doctor will tell you exactly how many tablets of Kisqali to take; in certain situations (e.g., in cases of kidney or liver problems), the doctor may instruct you to take a lower dosage of Kisqali, e.g., 400 mg (2 tablets of 200 mg), once daily or 200 mg (1 tablet of 200 mg), once daily.
- A treatment cycle lasts 28 days. Take Kisqali once a day, only on days 1 to 21 of a 28-day cycle.
  Do not take Kisqali on days 22-28 of the treatment cycle.

Do not exceed the recommended dose.

It is very important to follow the doctor's instructions. If you have certain side effects, the doctor may prescribe a lower dosage for you, interrupt the treatment with Kisqali, or stop it permanently.

Method of administration
Take Kisqali once daily at the same time each day, preferably in the morning. This will help you remember when to take the medicine.

Kisqali tablets should be swallowed whole (there is no information regarding crushing/halving/chewing). Do not take a tablet that is broken, cracked or otherwise damaged.

Duration of treatment
Take Kisqali once a day on days 1 to 21 of a 28-day treatment cycle.

Kisqali treatment is a long-term treatment. The doctor will regularly monitor your medical condition to check that the treatment is beneficial and not causing an undesirable effect. Continue treatment with Kisqali for as long as the doctor instructs you to.

If you accidentally took a higher dose of Kisqali
If you took an overdose, or if someone else accidentally swallowed the medicine, immediately refer to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you. Medical treatment may be necessary.

If you forgot to take Kisqali
If you vomited after taking a dose or forgot a dose, skip the dose that day. Take the next dose at the usual time. Do not take a double dose to make up for a forgotten dose. Instead, wait and take the next scheduled dose at the usual time.

Adhere to the treatment regimen as recommended by the doctor.

If you stop taking Kisqali
Stopping treatment with Kisqali may cause your condition to get worse. Do not stop treatment with the medicine without the doctor's instruction.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.
If you have further questions regarding use of the medicine, consult a doctor, pharmacist or nurse.

4. SIDE EFFECTS

As with any medicine, use of Kisqali may cause side effects in some users. Do not be alarmed by reading the list of side effects. You may not suffer from any of them.

Some side effects could be serious
Refer to a doctor immediately if any of the following effects occur during treatment with Kisqali. Also see section 2 "Before using the medicine".
- Fever, sweating or chills, cough, flu-like symptoms, weight loss, shortness of breath, blood in your phlegm, sores on your body, warm or painful areas on your body, diarrhoea or stomach pain, or feeling very tired (signs or symptoms of infections). *Very common (effects occurring in more than 1 in 10 users)*.
- Fever, chills, weakness and frequent infections, with symptoms, such as sore throat or mouth ulcers (signs of a low level leukocytes or lymphocytes, which are types of white blood cells). *Very common side effects (effects occurring in more than one in ten users)*.
- Abnormal blood test results, that provide information about the health of the liver (abnormal liver function results). *Very common side effects (effects occurring in more than one in ten users)*.
- Spontaneous bleeding or bruising (signs of a low level of blood platelets). *Common side effects (effects occurring in 1-10 in 100 users).*
- Sore throat or mouth sores with single episode of fever of at least 38.3°C or fever of over 38°C for more than one hour and/or with infection (febrile neutropenia). *Common side effects (effects occurring in 1-10 in 100 users).*
- Tiredness, itchy yellow skin or yellowing of the whites of the eyes, nausea or vomiting, loss of appetite, pain in the upper right side of the abdomen, dark or brown urine, bleeding or bruising occurring more easily than normal (these may be signs of a liver problem). *Common side effects (effects occurring in 1-10 in 100 users).*
- Reduced level of potassium in the blood, which could lead to disturbances in heart rhythm. *Common side effect (effect occurring in 1-10 in 100 users).*
- Chest pain or discomfort, changes in heart rate (fast or slow), palpitations, lightheadedness, fainting, dizziness, lips turning blue, shortness of breath, swelling (oedema) of the lower limbs or skin (these may be signs of heart problems). *Common side effects (effects occurring in 1-10 in 100 users).*
- Inflammation of the lungs, which can cause dry cough, chest pain, fever, shortness of breath and breathing difficulty (these may be signs of interstitial lung disease/ pneumonitis which, if severe, may be life threatening). *Common side effects (effects occurring in 1-10 in 100 users).*
- Serious infection with increased heart rate, shortness of breath or rapid breathing, fever and chills (these may be signs of sepsis which is an infection in the blood system that may be life-threatening). *Uncommon side effects (effects occurring in 1-10 in 1000 users).*
- A severe skin reaction which may include a combination of any of the following symptoms: rash, red skin, blistering of the lips, eyes or mouth, skin peeling, high fever, flu-like symptoms, enlarged lymph nodes (toxic epidermal necrolysis, TEN). *Side effects of unknown frequency (their frequency cannot be estimated from the available data).*

The doctor may ask you to take a lower dosage, interrupt the treatment with Kisqali, or stop it permanently.

Other possible side effects

Very common *(effects occurring in more than one in ten users)*
- Tiredness, pale skin (potential sign of a low level of red blood cells, anaemia)
- Sore throat, runny nose, fever (signs of a respiratory tract infection)
- Painful and frequent urination (signs of a urinary tract infection)
- Reduced appetite
- Headache
- Dizziness or light headedness
- Shortness of breath, breathing difficulties
- Cough
- Nausea
- Diarrhoea
- Vomiting
- Constipation
- Abdominal pain
- Mouth sores with gum inflammation (stomatitis)
- Upset stomach, indigestion, heartburn (discomfort or pains in the upper abdomen)
- Hair loss or hair thinning (alopecia)
- Rash
- Itching (pruritus)
- Back pain
- Tiredness (fatigue)
- Swollen hands, ankles or feet (peripheral oedema)
- Fever
- Weakness

Common *(effects occurring in 1-10 in 100 users)*
- Abdominal pain, nausea, vomiting and diarrhoea (signs of gastroenteritis, which is an infection of the gastrointestinal tract)
- Reduced level of calcium in the blood, which may sometimes lead to muscle cramps
- Reduced level of phosphate in the blood
- Spinning sensation (vertigo)
- Watery eyes
- Dry eyes
- Reduced level of potassium in the blood that may lead to heart rhythm disorders
- Strange taste in the mouth (dysgeusia)
- Dry skin
- Skin redness (erythema)
- Loss of skin colour in patches (vitiligo)
- Sore throat (oropharyngeal pain)
- Dry mouth
- Abnormal blood test result for kidney function (high level of creatinine in the blood)

Rare *(effects occurring in up to 1 in 1,000 users)*

A skin reaction that causes red spots or patches on the skin that may look like a "bullseye" with a dark red centre surrounded by paler red rings (erythema multiforme).

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Reporting side effects
Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il), that directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

You can also report to Novartis via the following e-mail address: Safetydesk.israel@novartis.com

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine and any other medicine should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) appearing on the package and tray (blister). The expiry date refers to the last day of that month.
- Do not store above 30°C.
- Do not use the medicine if you notice any damage to the package or signs of tampering.
- Do not discard medicines via the wastewater or household waste. Ask the pharmacist how to dispose of medicines no longer in use. These measures will help protect the environment.

6. FURTHER INFORMATION

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

Microcrystalline cellulose; low-substituted hydroxypropylcellulose; crospovidone (type A); magnesium stearate; poly (vinyl alcohol) - partially hydrolyzed; titanium dioxide (E171); talc; colloidal anhydrous silica; lecithin soya (E322); xanthan gum; iron oxide black (E172); iron oxide red (E172).

Each tablet contains 0.344 mg of soya lecithin.
See warning in section 2 "Before using the medicine" under "Important information about some of the ingredients of the medicine".

- What the medicine looks like and contents of the package:

Kisqali tablets are film-coated, round, curved with beveled edges, light grayish violet in colour, unscored, debossed with "RIC" on one side and "NVR" on the other side.

The tablets are packaged in blisters. Packages contain 21, 42 or 63 film-coated tablets.

Kisqali packages containing 63 tablets are intended for use by patients taking the full daily dosage, 600 mg ribociclib (3 tablets, once daily).
Kisqali packages containing 42 tablets are intended for use by patients taking the reduced daily dosage, 400 mg ribociclib (2 tablets, once daily).
Kisqali packages containing 21 tablets are intended for use by patients taking the lowest daily dosage, 200 mg ribociclib (1 tablet, once daily).

Not all package sizes may be marketed.

- Registration Holder and Importer and its address: Novartis Israel Ltd., P.O.B 7126, Tel Aviv.
- Registration Number of the medicine in the National Drug Registry of the Ministry of Health: 160-68-35298.

For some of the approved indications, the medicine is intended for women only.

Revised in July 2024.