

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

The medicine is dispensed with a doctor's prescription only

Calquence® Capsules

Composition:

Each capsule contains:

Acalabrutinib 100 mg

For inactive and allergenic ingredients, please refer to section 2 "Important information about some of the ingredients in this medicine" and section 6 - "Further Information".

Read this 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 you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.

1. WHAT IS THIS MEDICINE INTENDED FOR?

Calquence Capsules is indicated for the treatment of:

- adult patients with MCL (mantle cell lymphoma) who have received at least one prior therapy.
- adult patients with Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma (SLL).

Therapeutic group

BTK (Bruton tyrosine kinase) inhibitors.

2. BEFORE USING THE MEDICINE

Do not use this medicine if:

You are sensitive (allergic) to the active ingredient or to any of the other ingredients contained in the medicine (please refer to section 6 - "Further Information").

Special warnings regarding the use of Calquence Capsules:

Before treatment with Calquence Capsules tell your doctor if you:

- recently had surgery or plan to have surgery. Your doctor may stop treatment with Calquence Capsules for any planned surgical, medical, or dental procedure.
- have bleeding problems.
- have or had heart rhythm problems.
- have an infection or are at risk group for developing infections.
- have or had liver problems, including hepatitis B virus (HBV) infection.
- are pregnant or plan to become pregnant.
- are breastfeeding or plan to breastfeed.

Children and adolescents

There is no data regarding safety and efficacy of use of this medicine in children and adolescents.

Tests and follow up

In order to monitor your blood count, your doctor will refer you to do blood count test regularly during treatment with Calquence Capsules.

If you are on childbearing age, your doctor may do a pregnancy test before you start treatment with the medicine.

Drug interactions

If you are taking, or if you recently taken, other medicines including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. Taking Calquence Capsules with certain other medications may affect how Calquence Capsules works and may cause side effects. Especially tell your doctor if you are taking:

- A blood thinner medicine.
- Antacids and acid reducers from the H₂ receptor blocker group.

Medicines for reducing stomach acid:

- o Antacids – such as calcium carbonate
 - Take Calquence 2 hours before or 2 hours after you take these medicines
- o Histamine 2 receptor blockers - such as ranitidine and famotidine
 - Take Calquence 2 hours before you take these medicines
- o Proton pump inhibitors - such as omeprazole

- Avoid taking these medicines while you are taking Calquence

Use of the medicine and food

This medicine can be taken with or without food.

Pregnancy, breast-feeding and fertility:

Pregnancy

If you are pregnant, think you may be pregnant or planning to get pregnant, inform your doctor before taking this medicine. Calquence Capsules may hurt your fetus and cause problems during childbirth (dystocia). The doctor may ask you to do a pregnancy test before you start treatment with Calquence Capsules. If you are on childbearing age, you should use effective birth control (contraception) during treatment with Calquence Capsules and for at least 1 week after your final dose.

Breast-feeding

It is not known if Calquence Capsules passes into your breast milk. Do not breastfeed during treatment with Calquence Capsules and for at least 2 weeks after your final dose of Calquence Capsules.

Driving and using machines

Calquence Capsules has no or negligible effect on your ability to drive or use machines. However, if you feel dizziness, weakness or tiredness during treatment with Calquence Capsules, extra caution should be exercised when driving or using machines or tools.

Important information about some of the ingredients in this medicine

This medicine contains less than 1 mmol sodium (23 mg) per dose, i.e., it is essentially 'sodium-free'.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen in this medicine.

- The dosage and treatment regimen will be determined by the doctor only.

- The usual dosage is generally: one Calquence Capsule twice daily (about 12 hours apart).
- Do not change your dose or stop taking the medicine unless your doctor tells you to.
- Your doctor may instruct you to decrease your dose temporarily or completely stop taking the medicine if you develop certain side effects.
- **Do not exceed the recommended dose.**

How to take Calquence

- Can be taken with or without food.
- Swallow the capsule whole with a glass of water. Do not open and spread the capsule content. Do not break or chew the capsules.
- If you need to take antacid medicines, take it either 2 hours before or 2 hours after you take Calquence Capsules.
- If you need to take certain medicines called acid reducers (H₂ receptor blockers), take Calquence Capsules 2 hours before the acid reducer medicine.

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

If you have forgotten to take the medicine:

If you have forgotten to take the medicine at its scheduled time, take it as soon as you remembered. If it is more than 3 hours past your usual dosing time, skip the missed dose and take your next dose at your regularly scheduled time and consult the doctor. Do not take a double dose to make up for the forgotten dose.

Adhere to the treatment regimen as recommended by your doctor.

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

If you have any further questions regarding the use of the medicine, consult the doctor or the pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Calquence Capsules 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.

Effects that require special attention:

Refer to the doctor or hospital emergency room immediately if you experience any of the following serious side effects:

- **Serious infections** can happen during treatment with Calquence Capsules and may lead to death. Your doctor may prescribe for you certain medicines if you have an increased risk of getting infections. Tell your doctor immediately if you have any signs or symptoms of an infection, including fever, chills, or flu-like symptoms.
- **Bleeding problems** can happen during treatment with Calquence Capsules. **Bleeding problems** can be serious and may lead to death. Your risk of bleeding may increase if you are also taking a blood thinner medicine. Inform your doctor if you have any signs or symptoms of bleeding, including:
 - blood in your stools or black stools (looks like tar)
 - pink or brown urine
 - unexpected bleeding, severe bleeding or bleeding you cannot control
 - vomit blood or vomit that looks like coffee grounds
 - cough up blood or blood clots
 - dizziness
 - weakness
 - confusion
 - changes in your speech
 - headache that lasts a long time
 - bruising or red or purple skin marks
- **Decrease in blood cell counts** (decreased number of white blood cells, platelets, and red blood cells). Decrease in blood cell counts are common during treatment with Calquence Capsules, but can be severe. Your doctor should do blood tests to check your blood counts regularly during treatment with Calquence Capsules.
- **Second primary cancers.** New cancers have happened in patients during treatment with Calquence Capsules, including cancers of the skin or other organs. Your doctor will check you for skin cancers during treatment with Calquence Capsules. Use sunscreen when you are exposed to the sunlight.

- **Heart rhythm problems** have happened in people treated with Calquence Capsules, which may be serious or lead to death. Tell your doctor if you have any of the following signs or symptoms:
 - your heartbeat is fast or irregular
 - feeling dizzy or dizziness
 - feeling faint
 - shortness of breath
 - chest discomfort
- **Liver problems** can happen during treatment with Calquence Capsules, which may be severe or life-threatening, or lead to death. Contact your doctor if you experience stomach pain or discomfort, urine of dark color or yellowing of your skin. Your doctor will instruct to perform tests to monitor your liver function during treatment with Calquence Capsules.

Very common side effects, may affect more than 1 in 10 patients:

- Decrease in blood cell counts (platelets, white blood cells and red blood cells)
- headache
- diarrhea
- upper respiratory tract infection
- muscle and joint pain
- bruising

Common side effects, may affect 1-10 in 100 patients:

- Nausea
- Abdominal pain
- Constipation
- Vomiting
- Rash
- Bleeding
- Nose bleeding

These are not all of the possible side effects of Calquence.

If a side effect occurs, if any of the side effects worsens or if you suffer from a side effect not mentioned in this 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>

5. HOW SHOULD CALQUENCE CAPSULES BE STORED?

- Avoid poisoning! This medicine, and any other medicine, must 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. The expiry date refers to the last day of that month.
- Do not store above 30°C.

6. FURTHER INFORMATION

In addition to the active ingredient, Calquence Capsules also contains:

Silicified microcrystalline cellulose, partially pregelatinized starch, sodium starch glycolate Type A, magnesium stearate.

Capsule shell contains: gelatin, titanium dioxide, Iron oxide, yellow, Indigotine – FD&C Blue 2, Shellac glaze, Iron oxide black, Propylene glycol, Ammonium hydroxide 28%.

What does the medicine look like and what are the contents of the package

The pack contains 56 or 60 capsules in blister pack. The capsule has blue cap and yellow body, marked in black ink with ‘ACA 100mg’.

Not all pack sizes may be marketed.

Manufacturer: AstraZeneca AB, Södertälje, Sweden.

License holder and Importer: AstraZeneca (Israel) Ltd., 1 Atirei Yeda St., Kfar Saba 4464301.

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

163-15-35692-00

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