

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) – 1986

This medicine is dispensed with a doctor's prescription only

BRUKINSA 80 mg

Each capsule contains 80 mg of zanubrutinib

Inactive ingredients and allergens in the medicine: see 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.

Women: Should not become pregnant during treatment and for one week after receiving the last dose of BRUKINSA. You should use contraception during treatment and for one week after completing the last dose of BRUKINSA.

Men: You should avoid impregnating your partner during treatment and for one week after receiving the last dose of BRUKINSA. You should use contraception during treatment and for one week after receiving the last dose of BRUKINSA.

Use means of sun protection when you are exposed to sunlight.

1. What is this medicine intended for?

BRUKINSA is intended to treat adult patients with:

- Mantle cell lymphoma (MCL) who have received at least one prior therapy for their disease.
- Waldenström's macroglobulinemia (WM)

Therapeutic group - Anti-neoplastic agents, protein kinase inhibitors.

2. Before using this medicine

Do not use this medicine if:

- you are sensitive (allergic) to zanubrutinib or to any of the other ingredients of this medicine (see section 6, "**Additional information**").

Special warnings about using this medicine

Before the treatment with BRUKINSA, tell your doctor if:

- you have bleeding problems.
- your doctor may consider stopping the therapy with BRUKINSA 3-7 days pre- and post-surgery, medical or dental procedure.
- you have an infection.
- you have or had heart rhythm disorders.
- you have high blood pressure.

- you have liver problems, including a history of viral hepatitis B (HBV). **In case of severe hepatic impairment, your doctor may adjust the dose for you.**

Additional warnings it is important you know about:

Treatment with BRUKSINA may increase the risk of the following side effects:

- New cancers have happened in people during treatment with BRUKSINA, including skin cancer and cancer in other organs. Use sun protection when exposed to the sun.

Tests and follow-up

If you are of childbearing age, your doctor may ask you to do a pregnancy test before starting to use BRUKINSNA.

During treatment with BRUKINSNA, your doctor will take blood tests to monitor your blood count.

Drug interactions

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

- CYP3A enzyme inhibitors such as:
 - antifungal medicines, such as itraconazole or fluconazole.
 - antibiotic medicines, such as clarithromycin or erythromycin.
 - medicines to treat high blood pressure and angina pectoris – diltiazem.

Co-administration with one of the above medicines may raise the concentration of BRUKINSNA in the blood.

- CYP3A enzyme inducers such as:
 - type of antibiotic used to treat tuberculosis – rifampin.
 - an agent for the treatment of AIDS/HIV – efavirenz.

Co-administration of one of the following medicines may lower the concentration of BRUKINSNA in the blood.

If you are being treated with midazolam, a medicine administered for anesthetization, co-administration with BRUKINSNA may lower the concentration of midazolam in the blood.

If you are being treated with omeprazole, a medicine that reduces acid secretion in the stomach, co-administration with BRUKINSNA may lower the concentration of omeprazole in the blood.

If you are being treated with digoxin, which is administered for the treatment of various heart diseases, including arrhythmias, atrial fibrillation or heart failure, co-administration with BRUKINSNA may raise the concentration of digoxin in the blood.

Using this medicine and food

BRUKINSNA may be taken with or without food.

Pregnancy, breastfeeding and fertility

Pregnancy

This medicine may cause harm to a fetus. Women of childbearing age should avoid becoming pregnant prior to or during treatment with BRUKINSA and should use effective contraception during treatment with this medicine and for one week after taking the last dose.

Men must avoid impregnating women during treatment with BRUKINSA and for one week after receiving the last dose of BRUKINSA.

Breastfeeding

There are no data attesting to the presence of zanubrutinib in mother's milk or about the effect on milk production or on the breastfed infant. Because of the risk of serious side effects to a breastfed infant, it is recommended that women being treated with BRUKINSA should not breastfeed during treatment with the medicine and for two weeks after taking the last dose.

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:

160 mg twice daily or 320 mg once daily until disease progression or until side effects are observed that require discontinuation of the treatment.

Dosage adjustments may be likely when taking BRUKINSA with other medicines (see the **Drug interaction** section).

In cases of severe hepatic impairment, the recommended dosage is 80 mg twice daily.

Do not exceed the recommended dose.

How to take

Swallow the capsule whole, with a glass of water. Do not open, break or chew the capsule. Effectiveness of the product taken by opening, chewing or crushing the capsules has not been studied

If you have accidentally taken a higher dose

If you have taken an overdose, or if a child has accidentally swallowed some of the 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

If you forget to take this medicine at the scheduled time, do not take a double dose. Take the dose immediately on the same day and return to your regular treatment schedule the following day.

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 every 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 BRUKINSA may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Contact your doctor immediately if one or more of the following effects appear:

1. Bleeding – may be serious and lead to death. There is an increased risk of bleeding with concomitant use of blood thinner medicines.

Signs of bleeding:

- blood in stools (black stools)
- pink or brown urine
- unexpected bleeding, or severe bleeding that is uncontrollable
- bloody vomit or vomit that looks like coffee grounds
- coughing up blood or blood clots
- increased bruising
- dizziness
- weakness
- confusion
- changes in the mode of speaking
- prolonged headache

2. Infection – may be serious and lead to death.

Signs of infection:

- fever
- chills
- flu-like effects

3. Second Primary cancers (recurrence)

Patients who were treated with BRUKINSA developed new types of cancer, including skin cancer. Avoid exposure to sunlight.

4. Heart rhythm disorders (such as atrial fibrillation and atrial flutter). Signs:

- accelerated or irregular heartbeat
- dizziness
- fainting
- shortness of breath
- chest discomfort

5. Decrease in blood cell count (white blood cells, platelets and red blood cells) – Your doctor will refer you to tests to check your blood count during the period of treatment.

Very common side effects (affect more than one in ten users)

- neutropenia
- decrease in neutrophil count
- thrombocytopenia
- decrease in platelet count
- upper respiratory tract infection
- upper respiratory tract viral infection
- pneumonia
- fungal pneumonia
- cryptococcal pneumonia
- streptococcal pneumonia
- atypical pneumonia
- lower respiratory tract infection
- lower respiratory tract bacterial infection
- lower respiratory tract viral infection
- leukopenia
- decrease in white blood cell count
- anemia
- decrease in hemoglobin
- rash
- hematomas
- bruising
- diarrhea
- cough
- musculoskeletal pain
- back pain
- muscle pain
- joint pain
- arthritis
- urinary tract infection
- hematuria
- fatigue
- decrease in the potassium level in the blood
- constipation
- bleeding
- hypertension
- lymphocytosis
- elevated ALT levels
- elevated bilirubin
- nausea
- vomiting
- fever
- pruritus
- muscle spasms

- headache
- dizziness
- edema peripheral
- calcium decreased
- creatinine increased
- glucose increased
- potassium increased
- uric acid increased
- phosphate decreased

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

- major bleeding
- elevated uric acid level in the blood
- headaches

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.

Reporting side effects

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:

Store below 25°C.

6. Additional information

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

microcrystalline cellulose, gelatin, croscarmellose sodium, sodium lauryl sulphate, colloidal silicon dioxide, magnesium stearate, titanium dioxide.

What the medicine looks like and contents of the pack:

The medicine is packed in a bottle with a child-resistant cap containing 120 capsules. Each capsule is a white to off-white opaque capsule marked with "ZANU 80" in black color.

Registration holder's name and address:

Medison Pharma Ltd., 10 Hashiloach St., POB 7090, Petach-Tikva.

Manufacturer's name and address: BeiGene USA Inc., United States.

Revised in March 2022 according to MOH guidelines.

Registration number of the medicine in the Ministry of Health's National Drug Registry:
166-56-36452-99