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 avoid becoming pregnant during treatment and for one week after receiving the last dose of BRUKINSA. You should use effective birth control (contraception) during treatment and for one week after completing the last dose of BRUKINSA.

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

Breastfeeding: Do not breastfeed during treatment with BRUKINSA and for two weeks following 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).
- Relapsed or refractory marginal zone lymphoma (MZL) who have received at least one anti-CD20-based regimen.
- Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

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).
- you are pregnant or plan to become pregnant, BRUKINSA may harm your unborn baby.
- you are breastfeeding or plan to breastfeed. It is not known if BRUKINSA passes through breast milk.

Additional warnings it is important you know about:
Treatment with BRUKINSA may increase the risk of the following side effects:

- New cancers have been reported to appear during treatment with BRUKINSA, 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 BRUKINSA.
During treatment with BRUKINSA, 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 BRUKINSA in the blood.

Co-administration of one of the following medicines may lower the concentration of BRUKINSA 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.

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

Using this medicine and food
BRUKINSA 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 up to 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 – bleeding problems are common with BRUKINSA and can be serious and may lead to death. Your risk of bleeding may increase if you are also taking a 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, atrial flutter and ventricular arrhythmias, that can be serious and may lead to death). 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.
6. **Liver Problems - Liver problems, which may be severe or life-threatening, or lead to death, can happen in people treated with BRUKINSA. Your doctor will do blood tests to**

check your liver before and during treatment with BRUKINSA. Tell your doctor or get medical help right away if you have any signs of liver problems, including stomach pain or discomfort, dark-colored urine, or yellow skin and eyes.

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.

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

BRUKINSA-80mg-PIL-1024-V1