Package leaflet: Information for the patient

BRUKINSA 80 mg hard capsules
zanubrutinib

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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, 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What BRUKINSA is and what it is used for

BRUKINSA is an anticancer medicine that contains the active substance zanubrutinib. It belongs to a class of medicines called protein kinase inhibitors. This medicine works by blocking Bruton's tyrosine kinase, a protein in the body that helps cancer cells grow and survive. By blocking this protein, BRUKINSA reduces the number of cancer cells and slows down the worsening of the cancer.

BRUKINSA is used to treat Waldenström's macroglobulinaemia (also known as lymphoplasmacytic lymphoma), a cancer affecting a type of white blood cells called B lymphocytes that make too much of a protein called IgM. This medicine is used when the disease has come back, or treatment has not worked or in patients who cannot have chemotherapy together with an antibody.

BRUKINSA is also used to treat marginal zone lymphoma. This is a type of cancer that also affects B lymphocytes or B cells. In marginal zone lymphoma, the abnormal B cells multiply too quickly and live for too long. This may cause enlargement of organs that are part of the body's natural defences such as lymph nodes and spleen. The abnormal B cells may also affect various organs, such as stomach, salivary gland, thyroid, eyes, lungs, bone marrow and blood. Patients may have fever, weight loss, tiredness and night sweats, but also symptoms that depend on where the lymphoma develops. This medicine is used when the disease has come back, or treatment has not worked.

BRUKINSA is also used to treat chronic lymphocytic leukaemia (CLL), another type of cancer affecting B cells that involves the lymph nodes. This medicine is used in patients who have not previously been treated for CLL or when the disease has come back or has not responded to previous treatment.

BRUKINSA is also used to treat follicular lymphoma (FL). FL is a slow growing cancer that affects the B lymphocytes. When you have FL, you have too many of these B lymphocytes in your lymph nodes, spleen, and bone marrow. BRUKINSA is taken together with another medicine called 'obinutuzumab' when the disease has come back or when previously used medicines have not been effective.

2. What you need to know before you take BRUKINSA

Do not take BRUKINSA
if you are allergic to zanubrutinib or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before taking BRUKINSA:

- if you have ever had unusual bruising or bleeding or are on any medicines or supplements that increase your risk of bleeding (see section **"Other medicines and BRUKINSA"**). If you have had recent surgery or plan to have surgery, your doctor may ask you to stop taking BRUKINSA for a short time (3 to 7 days) before and after your surgery or dental procedure
- if you have an irregular heartbeat or have a history of irregular heartbeat or severe heart failure, or if you have any of the following: shortness of breath, weakness, dizziness, light-headedness, fainting or near fainting, chest pain or swollen legs
- if you have ever been advised that you are at higher risk of infections. You may experience viral, bacterial, or fungal infections during treatment with BRUKINSA with the following possible symptoms: fever, chills, weakness, confusion, body aches, cold or flu symptoms, feel tired or feel short of breath, yellowing of the skin or eyes (jaundice).
- if you have ever had or might have hepatitis B. This is because BRUKINSA could cause hepatitis B to become active again. Patients will be carefully checked by their doctor for signs of this infection before treatment is started
- if you have liver or kidney problems
- if you have recently had any surgery, especially if it might affect how you absorb food or medicines from your stomach or gut
- if you recently had low counts of red blood cells, infection-fighting cells or platelets in your blood
- if you had other carcinomas in the past including skin cancer (e.g., basal cell carcinoma or squamous cell carcinoma). Please use sun protection

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before taking this medicine.

Tests and check-ups before and during treatment
Laboratory tests may show lymphocytosis, an increase in white blood cells (lymphocytes) in your blood in the first few weeks of treatment. This is expected and may last for a few months. This does not necessarily mean that your blood cancer is getting worse. Your doctor will check your blood counts before and during the treatment and in rare cases the doctor may give you another medicine. Talk to your doctor about what your test results mean.

Tumour lysis syndrome (TLS): Unusual levels of chemicals in the blood caused by the fast breakdown of cancer cells have occurred during treatment of cancer and sometimes even without treatment. This may lead to changes in kidney function, abnormal heartbeat, or seizures. Your doctor or another healthcare provider may do blood tests to check for TLS.

Children and adolescents
BRUKINSA should not be used in children and adolescents, because it is unlikely to work.

Other medicines and BRUKINSA
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription, herbal medicines and supplements. This is because BRUKINSA may affect the way some medicines work. Also, some medicines can affect the way BRUKINSA works.

BRUKINSA may make you bleed more easily. This means you should tell your doctor if you take other medicines that increase your risk of bleeding. This includes medicines such as:

- acetylsalicylic acid (aspirin) and non-steroidal anti-inflammatories (NSAIDs) such as ibuprofen and naproxen,
- anticoagulants such as warfarin, heparin and other medicines for treating or preventing blood clots,
- supplements that may increase your risk of bleeding such as fish oil, vitamin E or flaxseed.

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before taking BRUKINSA.

Also tell your doctor if you take any of the following medicines – The effects of BRUKINSA or other medicines may be influenced if you take BRUKINSA together with any of the following medicines:

- antibiotics to treat bacterial infections – ciprofloxacin, clarithromycin, erythromycin, nafcillin or rifampicin
- medicines for fungal infections – fluconazole, itraconazole, ketoconazole, posaconazole, voriconazole
- medicines for HIV infection – efavirenz, etravirine, indinavir, lopinavir, ritonavir, telaprevir
- medicine to prevent nausea and vomiting associated with chemotherapy - aprepitant
- medicines for depression – fluvoxamine, St. John's wort
- medicine called kinase inhibitors for treatment of other cancers – imatinib
- medicines for high blood pressure or chest pain – bosentan, diltiazem, verapamil
- heart medicines/anti-arrhythmics – digoxin, dronedarone, quinidine
- medicines to prevent seizures, to treat epilepsy, or to treat a painful condition of the face called trigeminal neuralgia – carbamazepine, mephenytoin, phenytoin
- medicines for migraines and cluster headaches - dihydroergotamine, ergotamine
- medicine for extreme sleepiness and other sleep problems - modafinil
- medicine for psychosis and Tourette disorder - pimozide
- medicines for anaesthesia – alfentanil, fentanyl
- medicines called immunosuppressive agents – ciclosporin, sirolimus, tacrolimus

BRUKINSA with food
Grapefruit or Seville oranges (bitter oranges) should be consumed with caution around the time you take BRUKINSA. This is because they can increase the amount of BRUKINSA in your blood.

Pregnancy and breast-feeding
Do not get pregnant while you are taking this medicine. BRUKINSA should not be used during pregnancy. It is not known if BRUKINSA will harm your unborn baby.

Women of childbearing age must use a highly effective method of birth control during treatment with BRUKINSA and for least one month after treatment. A barrier method of contraception (e.g., condoms) must be used with hormonal contraceptives such as birth control pills or devices.

- Tell your doctor immediately if you become pregnant.

- Do not breast-feed while you are taking this medicine. BRUKINSA may pass into breast milk.

Driving and using machines
You may feel tired or dizzy after taking BRUKINSA, which may affect your ability to drive or use machines.

BRUKINSA contains sodium
BRUKINSA contains less than 1 mmol sodium (23 mg) per dose, that is to say 'essentially sodium-free'.

3. How to take BRUKINSA

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

The recommended dose is 320 mg (4 capsules) each day, *either* as 4 capsules once daily *or* 2 capsules in the morning and 2 in the evening.
Your doctor may adjust the dose.
Take the capsules by mouth with a glass of water with food or between meals.
Take the capsules about the same time each day.
BRUKINSA works best when it is swallowed whole. Therefore, swallow the capsules whole. Do not open, break or chew them.

If you take more BRUKINSA than you should
If you take more BRUKINSA than you should, talk to a doctor straight away. Take the capsule packet and this leaflet with you.

If you forget to take BRUKINSA
If you miss a dose, take it at the next scheduled time with a return to the normal schedule. If you take BRUKINSA once per day, take your next dose the following day. If you take the medicine twice a day, in the morning and in the evening and you forgot to take it in the morning, take your next dose in the evening. Do not take a double dose to make up for a forgotten capsule. If you are not sure, talk to your doctor, pharmacist or nurse about when to take your next dose.

If you stop taking BRUKINSA
Do not stop taking this medicine unless your doctor tells you.
If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

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

Stop taking BRUKINSA and tell a doctor straight away if you notice any of the following side effects:
itchy bumpy rash, difficulty breathing, swelling of your face, lips, tongue or throat – you may be having an allergic reaction to the medicine.

Tell a doctor straight away if you notice any of the following side effects:

Very common (may affect more than 1 in 10 people):

- fever, chills, body aches, feeling tired, cold or flu symptoms, being short of breath, frequent and painful urination – these could be signs of an infection (viral, bacterial or fungal). These could include infections of the nose, sinus or throat (upper respiratory tract infection), pneumonia, or urinary tract.
- bruising or increased tendency of bruising; contusions
- bleeding
- muscle and bone aches
- skin rash
- infection of the lung (lower respiratory tract infection)
- dizziness
- diarrhoea; your doctor may need to give you a fluid and salt replacement or another medicine
- cough
- fatigue
- high blood pressure
- constipation
- blood in urine
- blood tests showing a reduced number of blood cells. Your doctor should do blood tests during treatment with BRUKINSA to check the number of your blood cells.

Common (may affect up to 1 in 10 people):

- swollen hands, ankles or feet
- nosebleed
- itching of the skin
- small bleeding spots under the skin
- fast heart rate, missed heart beats, weak or uneven pulse, lightheadedness, shortness of breath, chest discomfort (symptoms of heart rhythm problems)
- weakness
- low white blood cell count with fever (febrile neutropenia)

Uncommon (may affect up to 1 in 100 people):

- reactivation of hepatitis B (if you had experienced hepatitis B, it may come back)
- intestinal bleeding (blood in stool)
- unusual levels of chemicals in the blood caused by the fast breakdown of cancer cells have occurred during treatment of cancer and sometimes even without treatment (tumour lysis syndrome)

Unknown:

- Redness and shedding of skin over a large area of the body, which may be itchy or painful (exfoliative dermatitis generalised)

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 to the Yellow Card Scheme. Website: 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 BRUKINSA

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 bottle after EXP. The expiry date refers to the last day of that month.
This medicine does not require any special storage conditions.

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 BRUKINSA contains

- The active substance is zanubrutinib. Each hard capsule contains 80 mg of zanubrutinib.
- The other ingredients are:
  - capsule content: microcrystalline cellulose, croscarmellose sodium, sodium lauryl sulfate (E487), silica colloidal anhydrous, magnesium stearate (see section 2 "BRUKINSA contains sodium").
  - capsule shell: gelatin and titanium dioxide (E171)
  - printing ink: shellac glaze (E904), iron oxide black (E172) and polypropylene glycol (E1520).

What BRUKINSA looks like and contents of the pack

BRUKINSA is a white to off-white hard capsule, marked with "ZANU 80" in black ink on one side. The capsules are provided in a plastic bottle with a child resistant closure. Each bottle contains 120 hard capsules.

Marketing Authorisation Holder

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Other sources of information

Detailed information on this medicine is available on the Medicines and Healthcare products Regulatory Agency web site: www.mhra.gov.uk