

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

This medicine is dispensed with a doctor's prescription only

Alunbrig® 30 mg

Alunbrig® 90 mg

Film-coated tablets

Name, form and strength of medicine

Active ingredient –

Alunbrig 30 mg: each film-coated tablet contains 30 mg of brigatinib.

Alunbrig 90 mg: each film-coated tablet contains 90 mg of brigatinib.

Inactive ingredients and allergens in this medicine – see section 2 under 'Important information about some of this medicine's ingredients', and 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.

This medicine is intended for adults.

1. What is this medicine intended for?

Alunbrig is indicated for the treatment of adult patients with metastatic (spread to other body parts) non-small cell lung cancer (NSCLC) positive for anaplastic lymphoma kinase (ALK) gene mutation (defect).

Therapeutic group: 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 in this medicine (see section 6).

Special warnings regarding the use of this medicine

Before beginning or during treatment with Alunbrig, tell your doctor if you have:

- Lung or breathing problems

- High blood pressure
- Slow heartbeat
- Any vision disturbance
- Current or previous pancreatitis
- Liver problems
- Diabetes or glucose intolerance
- Kidney problems or if you are on dialysis
- You are pregnant or plan to become pregnant (see more information under 'Pregnancy and breastfeeding')
- You are breastfeeding or plan to breastfeed (see more information under 'Pregnancy and breastfeeding')
- You are a man whose partner could become pregnant (see more information under 'Pregnancy and breastfeeding')
- You suffer from unexplained muscle pain, weakness or tenderness
- Photosensitivity:
Limit your time in the sun during treatment with **Alunbrig** and for at least 5 days after your final dose. **Alunbrig** may make your skin sensitive to sunlight. You may burn more easily and get severe burns.

When you are in the sun, wear a hat, protective clothing, and use a sunscreen and lip balm with a Sun Protection Factor (SPF) of 30 or greater to protect against sunburn.

Your doctor may need to adjust the dose you receive or stop treatment with **Alunbrig** temporarily or permanently.

Children and adolescents:

Efficacy and safety in children and adolescents under the age of 18 have not yet been determined.

Tests and follow-up:

Before and during the treatment with **Alunbrig**, your doctor will refer you for blood tests to monitor your blood sugar levels.

Before you start treatment with **Alunbrig**, 2 weeks after treatment initiation and at least once a month during the treatment, your doctor will check your blood pressure.

During the treatment with **Alunbrig**, your doctor will refer you for blood tests to monitor the CPK (an enzyme related to muscle activity) level and pancreatic enzymes level (amylase and lipase) in your blood.

During the treatment with **Alunbrig**, your doctor will check your heart rate.

During treatment, your doctor will order blood tests to check your blood levels of liver enzymes, particularly during the first three months of treatment.

Drug interactions:

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

- **itraconazole** to treat fungal infections
- **rifampicin** to treat tuberculosis
- **midazolam**, used as an anesthetic
- medicines that slow down your heart rate

Medicines may affect the level of **Alunbrig** in the blood or their level in the blood may be affected after taking **Alunbrig**.

Using this medicine and food:

Alunbrig can be taken with or without food.

Avoid eating grapefruit or drinking grapefruit juice during treatment with **Alunbrig**. Grapefruit may increase the level of the medicine in your blood.

Pregnancy, breastfeeding and fertility:

Pregnancy

- **Alunbrig** may harm your unborn baby. Tell your doctor immediately if you become pregnant during treatment with **Alunbrig**, if you think you may be pregnant or if you are planning to become pregnant.
Your doctor will determine via test whether or not you are pregnant before beginning treatment with **Alunbrig**.
- **Women** of childbearing age must use effective contraception during treatment with **Alunbrig** and for at least four months after the last dose of **Alunbrig**. Consult your doctor about the birth control methods that are right for you during treatment with **Alunbrig**.
- **Men**, whose female partners are of childbearing age, must use effective contraception during treatment with **Alunbrig** and for at least three months after the final dose of **Alunbrig**.

Breastfeeding

It is unknown if **Alunbrig** passes into breast milk. Do not breastfeed during treatment with **Alunbrig** and for one week after the final dose of **Alunbrig**.

Fertility

Alunbrig may cause fertility problems in men. This may affect your ability to father a child. Talk to your doctor if you have questions or concerns about fertility.

Driving and using machines:

Alunbrig may cause visual disturbances, dizziness or tiredness. Do not drive or operate dangerous machines if such signs occur.

Important information about some of this medicine's ingredients:

Alunbrig contains lactose.

Alunbrig 30 mg: each film-coated tablet contains 56.06 mg of lactose monohydrate.

Alunbrig 90 mg: each film-coated tablet contains 168.18 mg of lactose monohydrate.

If you have been told by your doctor that you have an intolerance to certain sugars, contact your doctor before starting treatment with this medicine.

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

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 usually is:

Your doctor will start you on a low dose of **Alunbrig** (90 mg once daily) for the first seven days of treatment and then increase the dose to 180 mg once daily.

Your doctor may change the dose, temporarily stop or permanently stop treatment with **Alunbrig** due to any side effects that may appear or if you suffer from liver or kidney problems.

Take **Alunbrig** once daily.

Alunbrig can be taken with or without food.

Do not exceed the recommended dose.

Swallow the **Alunbrig** tablet whole. Do not crush/split/chew the tablet as it is film coated.

If you have accidentally taken a higher dose or if a child has accidentally swallowed 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 at the required time, do not take a double dose. Take your next dose of **Alunbrig** at your regular scheduled time and consult your doctor.

If you vomit after taking a dose of the medicine, do not take an extra dose. Take your next dose of **Alunbrig** at your regular scheduled time.

Adhere to the treatment as recommended by your doctor.

Even if your health improves, do not stop taking this medicine without consulting your doctor.

If you stop taking this medicine

Do not change your dose, and do not stop taking **Alunbrig** before talking to your doctor.

Do not take medicines in the dark! Check the label and dose each 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 any medicine, using **Alunbrig** may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of them.

Alunbrig may cause serious side effects, including:

- **Lung problems (Interstitial Lung Disease (ILD)/pneumonitis)** - occur in 1-10 in 100 users. **Alunbrig may cause severe or life-threatening swelling/edema (inflammation) of the lungs any time during treatment and may lead to death.** These lung problems occur particularly within the first week of treatment with **Alunbrig**. The symptoms may be similar to symptoms caused by lung cancer. **Tell your doctor immediately** if you experience any new symptoms or worsening of existing symptoms, including:
 - trouble breathing or shortness of breath
 - cough with or without mucus
 - chest pain
 - fever
- **High blood pressure (hypertension)** - occurs in more than one in 10 users. **Alunbrig** may cause high blood pressure. Your doctor will check your blood pressure before starting and during treatment with **Alunbrig**. **Tell your doctor immediately** if you experience headaches, dizziness, blurred vision, chest pain or shortness of breath.
- **Slow heart rate (bradycardia)** - occurs in more than one in 10 users. **Alunbrig** may cause very slow heart rate, a condition that can be severe. Your doctor will check your heart rate during treatment with **Alunbrig**. **Tell your doctor immediately** if you feel dizzy, lightheaded or faint during treatment with **Alunbrig**. Tell your doctor if you are treated with heart rate or blood pressure medicines.
- **Photosensitivity** - occurs in 1-10 in 100 users. Tell your doctor if you develop any skin reaction.
- **Vision problems** - occur in 1-10 in 100 users. **Alunbrig** may cause vision problems. Your doctor may stop treatment with **Alunbrig** and refer you to an eye specialist if you develop severe vision problems during treatment with **Alunbrig**. **Tell your doctor immediately** if you experience any loss of vision or any change in vision, including:
 - double vision
 - light hurting your eyes
 - seeing flashes of light
 - new or increased floaters
 - blurry vision

- **Muscle pain, tenderness, and weakness (myalgia)** - occur in more than one in 10 users.

Alunbrig may increase the level of an enzyme in your blood called creatine phosphokinase (CPK), a condition which may be a sign of muscle damage. Your doctor will refer you for blood tests to check your blood level of CPK during treatment with **Alunbrig**. **Tell your doctor immediately** if you experience new or worsening signs and symptoms of muscle problems, including unexplained muscle pain or muscle pain that does not go away, tenderness, or weakness.

- **Inflammation of the pancreas (pancreatitis)** - occurs in more than one in 10 users.

Alunbrig may increase the levels of enzymes in your blood called amylase and lipase, a condition that may be a sign of pancreatitis. Your doctor will refer you for blood tests to monitor your pancreatic enzyme blood levels during treatment with **Alunbrig**. **Tell your doctor immediately** if you experience new or worsening signs or symptoms of pancreatitis, including upper abdominal pain that may spread to the back and get worse with eating, weight loss, or nausea.

- **Liver problems (hepatotoxicity)** - occur in more than one in 10 users.

Alunbrig may increase the levels of bilirubin in your blood and of enzymes called aspartate aminotransferase (AST) and alanine aminotransferase (ALT) in your blood, which may be a sign of liver problems. Your doctor will order blood tests to check your liver during treatment with **Alunbrig**. **Tell your doctor right away** if you get new or worsening signs or symptoms of hepatotoxicity, including:

- yellowing of your skin or the white part of your eyes
- dark (tea color) urine
- nausea or vomiting
- pain on the right side of your stomach area
- bleed or bruise more easily than normal
- itchy skin
- decreased appetite
- feeling tired

- **High blood sugar (hyperglycemia)** - occurs in more than one in 10 users.

Alunbrig may increase your blood sugar levels. Your doctor will refer you for blood tests to monitor your blood sugar levels before starting and during treatment with **Alunbrig**. Your doctor may start or change the medication therapy you already receive to control your blood sugar levels. **Tell your doctor immediately** if you experience new or worsening signs or symptoms of hyperglycemia, including:

- increased feeling of thirst
- feeling sick to your stomach
- needing to urinate more than usual
- feeling weak or tired
- increased feeling of hunger
- feeling confused

Additional side effects

Tell your doctor or pharmacist if you notice any of the following side effects:

Very common side effects (appear in more than one in 10 users):

- pneumonia
- nausea
- fatigue
- weakness
- dizziness
- edema
- headache
- diarrhea
- cough
- vomiting
- constipation
- inflammation of the oral cavity (stomatitis)
- rash
- skin itching
- shortness of breath
- trouble breathing
- spasms (muscle spasms)
- back pain
- muscle pain
- joint pain
- peripheral neuropathy/peripheral prickling sensation (paresthesia) (peripheral nervous system disorders)
- liver function disorder (elevation of levels of liver enzymes AST and ALT in your blood)
- increased blood level of the enzyme creatine phosphokinase (CPK)
- increased blood level of the enzyme alkaline phosphatase (ALP)
- increased blood level of creatinine
- anemia
- reduced blood level of phosphorus
- reduced blood level of magnesium
- increased or reduced blood level of calcium
- reduced albumin level
- increased levels of lipase and amylase
- reduced blood level of sodium
- reduced or increased blood level of potassium
- low count of white blood cells called lymphocytes (lymphopenia) and neutrophils (neutropenia)
- fever
- abdominal pain
- increased blood pressure
- high blood levels of insulin
- increased blood level of cholesterol

- insomnia

Common side effects (appear in 1-10 in 100 users):

- reduced platelet count in the blood, which may increase the risk of bleeding and bruising
- changes in sense of taste
- indigestion
- abdominal distention
- dry skin
- pain in arms and legs
- muscle and joint stiffness
- pain
- pulmonary embolism
- common cold
- urinary tract infection
- decreased appetite

Uncommon side effects (appear in 1-10 in 1,000 users):

reflux

Additional side effects of unknown frequency

increased blood level of bilirubin

sudden death, respiratory failure, bacterial meningitis and sepsis caused by infection of the urinary tract.

These are not all of the possible side effects of **Alunbrig**. For further information, contact your doctor or pharmacist.

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

Side effects can be reported to the Ministry of Health by clicking on the link 'Reporting Side Effects of Drug Treatment' found on the Ministry of Health home page (www.health.gov.il) which directs you to the online form for reporting side effects or by entering the link:

<https://sideeffects.health.gov.il>

5. How to store the medicine?

- Prevent poisoning! This medicine and any other medicine should be kept in a closed place out of the sight and reach of children and/or infants in order to prevent poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor.

- Do not use the medicine after the expiry date (exp. date) stated on the bottle/carton. The expiry date refers to the last day of that month.
- After first opening, the medicine can be used for 60 days and no later than the expiry date of the product.

Storage conditions

- Do not store above 30°C.
- The product bottle contains a desiccant sachet within. Please leave the desiccant sachet in the bottle. Do not swallow it.

6. Additional information

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

microcrystalline cellulose, lactose monohydrate, sodium starch glycolate (Type A), magnesium stearate, hydrophobic colloidal silica.

The coating of the tablet contains:

talc, polyethylene glycol, polyvinyl alcohol and titanium dioxide.

What the medicine looks like and contents of the pack:

Alunbrig 30 mg: Round, white to off-white film-coated tablet with debossed "U3" on one side and plain on the other side.

Available in bottles containing 30 tablets.

Alunbrig 90 mg: Oval, white to off-white film-coated tablet with debossed "U7" on one side and plain on the other side.

Available in bottles containing 7 or 30 tablets.

Not all pack sizes may be marketed.

Registration holder: Takeda Israel Ltd., 25 Eyal St., P.O. Box 4140, Petach Tikva 4951125.

Manufacturer: Takeda Pharma A/S Delta Park 45, 2665 Vallensbaek Strand, Denmark.

Revised in April 2023 according to MOH guidelines.

Registration number of the medicine in the Ministry of Health's National Drug Registry:
161-06-35335, 161-05-35334