**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 – 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)-positive 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

- Lung problems, some severe, are more frequent within the first 7 days of treatment. Symptoms may be similar to symptoms from lung cancer. Tell your doctor of any new or worsening symptoms of the disease, including difficulty breathing, shortness of breath, chest pain, cough and fever.
- High blood pressure
- Slow heartbeat
- Any vision disturbance
- Current or previous pancreatitis
- Diabetes or glucose intolerance
- Liver problems
- Kidney problems or if you are on dialysis
- If 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.

**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:

- **ketoconazole, itraconazole, voriconazole**: medicines to treat fungal infections
- **indinavir, nelfinavir, ritonavir, saquinavir**: medicines to treat HIV

- **clarithromycin, telithromycin, troleandomycin**: medicines to treat bacterial infections
- **nefazodone**: a medicine to treat depression
- **St. John's wort**: a herbal product to treat depression
- **carbamazepine**: a medicine to treat various neurological conditions
- **phenobarbital, phenytoin**: medicines to treat epilepsy
- **rifabutin, rifampicin**: medicines to treat tuberculosis
- **digoxin**: a medicine to treat heart problems
- **dabigatran**: a medicine to inhibit blood clotting
- **colchicine**: a medicine to treat gout attacks
- **pravastatin, rosuvastatin**: medicines to treat elevated cholesterol levels
- **methotrexate**: a medicine to treat severe joint inflammation, cancer and psoriasis
- **sulfasalazine**: a medicine to treat severe bowel and joint inflammation
- **efavirenz, etravirine**: medicines to treat HIV
- **modafinil**: a medicine to treat narcolepsy
- **bosentan**: a medicine to treat pulmonary hypertension
- **nafcillin**: a medicine to treat bacterial infections
- **alfentanil, fentanyl**: medicines to treat pain
- **quinidine**: a medicine to treat irregular heart rhythm
- **cyclosporine, sirolimus, tacrolimus**: medicines to suppress the immune system

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

- Medicines which may increase **Alunbrig** blood concentrations - such as anti-viral agents, anti-fungal agents and macrolide antibiotics.
- Medicines which may decrease **Alunbrig** blood levels - such as medicines to treat tuberculosis, medicines to treat various neurological conditions, medicines to treat epilepsy and St. John's wort (to treat mild depression).

**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 and sodium.

**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.

## 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 <u>each time</u> 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. <u>Side effects</u>

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/oedema (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 1 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 1-10 in 100 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
  - sensitivity to light
  - seeing flashes of light
  - new or increased floaters
  - blurry vision

- **Muscle pain, tenderness, and weakness (myalgia)** - occur in more than 1 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 1 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.

- **High blood sugar (hyperglycaemia)** - occurs in more than 1 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 hyperglycaemia, 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 1 in 10 users):
- pneumonia
- cold-like symptoms
- nausea
- fatigue
- weakness
- dizziness
- oedema
- headache
- diarrhoea
- cough
- vomiting
- constipation
- inflammation of the oral cavity (stomatitis)
- rash
- skin itching
- decreased appetite
- shortness of breath
- trouble breathing
- blood clotting disorder
- spasms (muscle spasms)
- back pain
- muscle pain
- joint pain
- peripheral neuropathy/peripheral prickling sensation (paraesthesia) (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 (may indicate reduced kidney function)
- anaemia
- reduced blood level of phosphorus
- reduced blood level of magnesium
- increased or reduced blood level of calcium
- reduced albumin level
- reduced blood level of sodium

- reduced blood level of potassium
- low count of white blood cells called lymphocytes (lymphopaenia) and neutrophils (neutropaenia)
- fever
- abdominal pain
- increased blood pressure
- high blood levels of insulin

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
- insomnia
- memory impairment
- change in sense of taste
- abnormal electrical activity of the heart (prolonged electrocardiogram QT interval)
- rapid heartbeat (tachycardia)
- palpitations
- dry mouth
- indigestion
- abdominal distention
- increased blood level of lactate dehydrogenase – may indicate tissue damage
- increased blood level of bilirubin
- dry skin
- sensitivity to sunlight
- musculoskeletal chest pain
- pain in arms and legs
- muscle and joint stiffness
- pain
- increased blood level of cholesterol
- weight loss
- decreased level of oxygen in body tissues

Additional side effects of unknown frequency
Sudden death, respiratory failure, pulmonary embolism, 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 Following 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 Efal St., P.O. Box 4140, Petach Tikva 4951125.

**Manufacturer:** ARIAD Pharmaceuticals Inc., Cambridge, Massachusetts, USA.

**Revised in October 2021 according to MOH guidelines.**

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