Information for the user
BEIGANI 30mg/90mg film-coated tablets
Brigatinib

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 BEIGANI is and what it is used for

BEIGANI is a drug used to treat a type of lung cancer called non-small cell lung cancer (NSCLC) that is advanced (metastatic). It is to be used in patients who have a specific gene mutation in the anaplastic lymphoma kinase (ALK) gene. It should be used in patients whose cancer has worsened after, or who could not tolerate treatment with, another drug called crizotinib.

BEIGANI is a prescription medicine used to treat people with non-small cell lung cancer (NSCLC): that has a certain type of abnormal anaplastic lymphoma kinase (ALK) gene, **and**
that has spread to other parts of your body, **and**
who have taken the medicine crizotinib, but their NSCLC worsened or they cannot tolerate taking crizotinib.

It is not known if BEIGANI is safe and effective in children.

BEIGANI can be prescribed to you if your disease is at an advanced stage and previous treatment has not helped to stop your disease.

BEIGANI may slow or stop the growth of lung cancer. It may help shrink tumours.

If you have any questions about how BEIGANI works or why this medicine has been prescribed for you, ask your doctor.

2. What you need to know before you take BEIGANI

Do not take BEIGANI
▪ If you are allergic to Brigatinib or any of the other ingredients of this medicine (listed in Section 6, "What BEIGANI contains").

▪Avoid eating grapefruit or drinking grapefruit juice during treatment with BEIGANI. Grapefruit may increase the amount of BEIGANI in your blood.

▪ Warnings and precautions

Before you take BEIGANI, tell your healthcare provider about all of your medical conditions, including if you:
▪ have lung or breathing problems
▪ have high blood pressure
▪ have a slow heartbeat
▪ have any vision problems
▪ have or have had pancreatitis
▪ have diabetes mellitus or glucose intolerance
▪ are pregnant or plan to become pregnant. BEIGANI can harm your unborn baby. Tell your healthcare provider right away if you become pregnant during treatment with BEIGANI or think you may be pregnant.
▪**Females** who are able to become pregnant should use effective non-hormonal birth control during treatment with BEIGANI and for at least 4 months after the final dose of BEIGANI. Birth control pills (oral contraceptives) and other hormonal forms of birth control may not be effective if used during treatment with BEIGANI. Talk to your healthcare provider about birth control choices that are right for you during treatment with BEIGANI.
▪ **Males** who have female partners that are able to become pregnant should use effective birth control during treatment with BEIGANI and for at least 3 months after the final dose of BEIGANI.
▪ are breastfeeding or plan to breastfeed. It is not known if BEIGANI passes into your breast milk.
Do not breastfeed during treatment with BEIGANI and for 1 week after the final dose of BEIGANI.

Tell your healthcare provider about all the medicines you take, including prescription medicines, over-the-counter medicines, vitamins, or herbal supplements.

Pediatric Use
The safety and efficacy of BEIGANI in pediatric patients have not been established.

Geriatric Use
No clinically relevant differences in safety or efficacy were observed between patients ≥65 years and younger patients.

Hepatic Impairment
No dose adjustment is recommended for patients with mild hepatic impairment (total bilirubin within upper limit of normal [ULN] and AST greater than ULN or total bilirubin greater than 1 and up to 1.5 times ULN and any AST). The pharmacokinetics and safety of BEIGANI in patients with moderate or severe hepatic impairment have not been studied

Renal Impairment
No dose adjustment is recommended for patients with mild and moderate renal impairment [creatinine clearance (CLcr) 30 to 89 mL/min estimated by Cockcroft-Gault)]. The pharmacokinetics and safety of BEIGANI in patients with severe renal impairment (CLcr 15 to 29 mL/min estimated by Cockcroft-Gault) have not been studied

Other medicines and BEIGANI
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including herbal medicines and medicine obtained over the counter.
In particular, the following medicines may increase the risk of side effects with BEIGANI:
▪ strong CYP3A inhibitors including but not limited to certain antivirals (e.g., boceprevir, cobicistat, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir)
macrolide antibiotics (e.g., clarithromycin)
antifungals (e.g., itraconazole, ketoconazole, posaconazole, voriconazole)
conivaptan.

Avoid grapefruit or grapefruit juice as it may also increase plasma concentrations of brigatinib.

If concomitant use of a strong CYP3A inhibitor cannot be avoided, reduce the dose of BEIGANI by approximately 50%

The following medicines may reduce the effectiveness of BEIGANI:
strong CYP3A inducers including but not limited to rifampin, carbamazepine, phenytoin, and St. John's Wort.

▪ The following medicines t May Have Their Plasma Concentrations Altered by Brigatinib:
Coadministration of BEIGANI with CYP3A substrates, including hormonal contraceptives, can result in decreased concentrations and loss of efficacy of CYP3A substrates

Females and Males of Reproductive Potential
BEIGANI can cause fetal harm

Females
Advise females of reproductive potential to use effective non-hormonal contraception during treatment with BEIGANI and for at least 4 months after the final dose. Counsel patients to use a non-hormonal method of contraception since BEIGANI can render some hormonal contraceptives ineffective.

Males
Because of the potential for genotoxicity, advise males with female partners of reproductive potential to use effective contraception during treatment with BEIGANI and for at least 3 months after the final dose.

Infertility
Based on findings in male reproductive organs in animals, BEIGANI may cause reduced fertility in males.

BEIGANI with food and drink
You can take BEIGANI with or without food; however, you should avoid drinking grapefruit juice or eating grapefruit while on treatment with BEIGANI as they may change the amount of BEIGANI in your body.

There are no data regarding the secretion of brigatinib in human milk or its effects on the breastfed infant or milk production. Because of the potential for adverse reactions in breastfed infants, advise lactating women not to breastfeed during treatment with BEIGANI and for 1 week following the final dose.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines

You should take special care when driving and using machines as patients taking BEIGANI may experience visual disturbances, dizziness, and tiredness.

3. How to take BEIGANI

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.
▪ Take BEIGANI exactly as your healthcare provider tells you to take it. Do not change your dose or stop taking BEIGANI unless your healthcare provider tells you to.
▪ Your healthcare provider will start you on a low dose (90 mg) of BEIGANI for the first 7 days of treatment. If you tolerate this dose of BEIGANI well, your healthcare provider may increase your dose after the first 7 days of treatment.
The recommended dosing regimen for BEIGANI is:
▪ 90 mg orally once daily for the first 7 days;
▪ if 90 mg is tolerated during the first 7 days, increase the dose to 180 mg orally once daily.
Your healthcare provider may change your dose, temporarily stop, or permanently stop treatment with BEIGANI if you have side effects.
If BEIGANI is interrupted for 14 days or longer for reasons other than adverse reactions, resume treatment at 90 mg once daily for 7 days before increasing to the previously tolerated dose.
▪ Take BEIGANI 1 time each day.
▪ Take BEIGANI with or without food.
▪ Swallow BEIGANI tablets whole. Do not crush or chew tablets.
▪ If you miss a dose of BEIGANI, do not take the missed dose. Take your next dose at your regular time.
▪ If you vomit after taking a dose of BEIGANI, do not take an extra dose. Take your next dose at your regular time.
If you accidentally take too many of this medicine, tell your doctor or pharmacist right away. You may require medical attention.

If you stop taking BEIGANI
It is important to take BEIGANI every day, as long as your doctor prescribes it to you. If you are not able to take the medicine as your doctor prescribed, or you feel you do not need it anymore, contact your doctor right away.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

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

If you experience any side effects, talk to your doctor, pharmacist, or nurse. This includes any possible side effects not listed in this leaflet.

Some side effects could be serious. You should immediately contact your doctor if you experience any of the following serious side effects (see also section 2 "What you need to know before you take BEIGANI "):
▪ **Lung problems. BEIGANI may cause severe or life-threatening swelling (inflammation) of the lungs anytime during treatment, and can lead to death**. These lung problems happen especially **within the first week of treatment** with BEIGANI. Symptoms may be similar to those symptoms from lung cancer. Tell your healthcare provider right away if you have any new or worsening symptoms, including:
▪ trouble breathing or shortness of breath
▪ chest pain
▪ cough with or without mucous
▪ fever

High blood pressure (hypertension). BEIGANI may cause high blood pressure. Your healthcare provider will check your blood pressure before starting and during treatment with BEIGANI. Tell your healthcare provider right away if you get headaches, dizziness, blurred vision, chest pain or shortness of breath.

Slow heart rate (bradycardia). BEIGANI may cause very slow heartbeats that can be severe. Your healthcare provider will check your heart rate during treatment with BEIGANI. Tell your healthcare provider right away if you feel dizzy, lightheaded, or faint during treatment with BEIGANI. Tell your healthcare provider if you start to take or have any changes in heart or blood pressure medicines.

▪ **Vision problems.** BEIGANI may cause vision problems. Your healthcare provider may stop BEIGANI and refer you to an eye specialist if you develop severe vision problems during treatment with BEIGANI. Tell your healthcare provider right away if you have any loss of vision or any change in vision, including:
▪ double vision
▪ seeing flashes of light
▪ blurry vision
▪ light hurting your eyes
▪ new or increased floaters

▪ **Muscle pain, tenderness, and weakness (myalgia).** BEIGANI may increase the level of an enzyme in your blood called creatine phosphokinase (CPK), which may be a sign of muscle damage. Your healthcare provider will do blood tests to check your blood levels of CPK during treatment with BEIGANI. Tell your healthcare provider right away if you get 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).** BEIGANI may increase enzymes in your blood called amylase and lipase, which may be a sign of pancreatitis. Your healthcare provider will do blood tests to check your pancreatic enzyme blood levels during treatment with BEIGANI. Tell your healthcare provider right away if you get new or worsening signs and 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 (hyperglycemia).** BEIGANI may increase your blood sugar levels. Your healthcare provider will do blood tests to check your blood sugar levels before starting and during treatment with BEIGANI. Your healthcare provider may need to start or change your blood sugar medicine to control your blood sugar levels. Tell your healthcare provider right away if you get new or worsening signs and symptoms of hyperglycemia, including:
▪ feeling very thirsty
▪ needing to urinate more than usual
▪ feeling very hungry
▪ feeling sick to your stomach
▪ feeling weak or tired
▪ feeling confused

▪ **The most common side effects of BEIGANI include:**
▪ nausea
▪ diarrhea
▪ fatigue
▪ cough
▪ headache

BEIGANI may cause fertility problems in males. This may affect your ability to father a child. Talk to your healthcare provider if you have concerns about fertility.
These are not all of the possible side effects of BEIGANI. For more information, ask your healthcare provider or pharmacist.▪

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store BEIGANI
▪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 bottle or blister foil and carton after "EXP".
▪ Store at controlled room temperature 20°C to 25°C (68°F to 77°F); excursion permitted between 15°C to 30°C (59°F to 86°F)
▪ Do not use any pack that is damaged or shows signs of tampering.

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 BEIGANI contains
The active substance in BEIGANI is Brigatinib, kinase inhibitor. The chemical name for brigatinib is 5-chloro-N4-[2-(dimethylphosphoryl)phenyl]-N2-{2-methoxy-4[4-(4-methylpiperazin-1-yl)piperidin-1-yl]phenyl}pyrimidine-2,4-diamine. The molecular formula is C29H39ClN7O2P which corresponds to a formula weight of 584.10 g/mol. Brigatinib has no chiral centers. The chemical structure is shown below:

Brigatinib is an off-white to beige/tan solid.
BEIGANI is supplied for oral use as film-coated tablets containing 30 mg or 90 mg of brigatinib.
The other ingredients are:
lactose monohydrate, microcrystalline cellulose, sodium starch glycolate (Type A), magnesium stearate, and hydrophobic colloidal silica.
The tablet coating consists of talc, polyethylene glycol, polyvinyl alcohol, and titanium dioxide.

What BEIGANI looks like and contents of the pack
▪ 30 mg, round, white to off-white film-coated tablet with "TLPH" debossed on one side, Bottles or blister strips of 21 tablets.

▪ 90 mg, oval, white to off-white film-coated tablet with "TLPH" debossed on one side, Bottles or blister strips of 21 tablets.
Not all pack sizes may be marketed.

Marketing Authorisation Holder
Tongmeng(Lao) Pharmaceutical **and Food** Co., Ltd
Rd13 South,31km,Ban Naphasuk,Saithany District
Vientiane
Lao PDR

Manufacturer
Tongmeng(Lao) Pharmaceutical **and Food** Co., Ltd
Rd13 South,31km,Ban Naphasuk,Saithany District
Vientiane
Lao PDR

For any information about this medicine, please contact the local representative of the Marketing.

TLPH