ALUNBRIG® ▼(brigatinib) PRESCRIBING INFORMATION FOR REPUBLIC OF IRELAND

Refer to Summary of Product Characteristics (SmPC) before prescribing

Presentation: Brigatinib 180 mg, 90 mg and 30 mg film-coated tablets. **Indications:** As monotherapy for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously not treated with an ALK inhibitor. As monotherapy for the treatment of adult patients with ALK-positive advanced NSCLC previously treated with crizotinib. **Dosage and administration:** Recommended starting dose is 90 mg once daily for the first 7 days, then 180 mg once daily. If ALUNBRIG is interrupted for 14 days or longer for reasons other than adverse reactions, treatment should be resumed at 90 mg once daily for 7 days before increasing to the previously tolerated dose. If a dose is missed or vomiting occurs after taking a dose, an additional dose should not be administered and the next dose should be taken at the scheduled time. Treatment should continue as long as clinical benefit is observed. Dosing interruption and/or dose reduction may be required. Refer to SmPC for full dose adjustments. Paediatric population: No data are available. Elderly patients: Dose adjustment is not required. No available data on patients aged > 85 years. Hepatic impairment: A reduced starting dose of 60 mg once daily for the first 7 days, then 120 mg once daily is recommended for patients with severe hepatic impairment (Child Pugh class C). Renal impairment: A reduced starting dose of 60 mg once daily for the first 7 days, then 90 mg once daily is recommended for patients with severe renal impairment (eGFR <30 mL/min). Patients with severe renal impairment should be closely monitored for new or worsening respiratory symptoms (e.g., dyspnoea, cough, etc.) particularly in the first week. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. **Warnings and precautions:** Refer to SmPC for recommended dose modifications. Pulmonary adverse reactions: Most occurred within the first 7 days of treatment, but they can occur later in treatment. Patients should be monitored for new or worsening respiratory symptoms (e.g., dyspnoea, cough, etc.), particularly in the first week of treatment. If interstitial lung disease/ pneumonitis is suspected, the dose of ALUNBRIG should be withheld, and the patient evaluated for other causes of symptoms (e.g., pulmonary embolism, tumour progression, and infectious pneumonia). Dose modification may be required. Hypertension: Heart rate and blood pressure should be monitored regularly. Hypertension should be treated according to standard guidelines. Heart rate should be monitored more frequently in patients if concomitant use of a medicinal product known to cause bradycardia cannot be avoided. Withhold ALUNBRIG in patients with severe hypertension (≥ Grade 3) until hypertension has recovered to Grade 1 or to baseline. Modify dose accordingly. Bradycardia: Caution should be exercised when administering ALUNBRIG in combination with other agents known to cause bradycardia. If symptomatic bradycardia occurs, treatment with ALUNBRIG should be withheld and concomitant medicinal products known to cause bradycardia should be evaluated. Upon recovery, the dose should be modified according to SmPC. In case of life-threatening bradycardia, if no contributing concomitant medication is identified or in case of recurrence, treatment with ALUNBRIG should be discontinued. Visual disturbance: Advise patients to report any visual symptoms. Consider ophthalmologic evaluation/dose reduction for new or worsening severe symptoms. Creatine phosphokinase (CPK) elevation: Patients should be advised to report any unexplained muscle pain, tenderness, or weakness. CPK levels should be monitored regularly during ALUNBRIG treatment. Based on the severity of the CPK elevation, and if associated with muscle pain or weakness, treatment with ALUNBRIG should be withheld, and the dose modified. Elevations of pancreatic enzymes: Lipase and amylase should be monitored regularly during treatment with ALUNBRIG. Based on the severity of the laboratory abnormalities, treatment with ALUNBRIG should be withheld, and the dose modified. Hepatotoxicity: Liver function, including aspartate aminotransferase (AST), alanine aminotransferase (ALT) and total bilirubin should be assessed prior to the initiation of ALUNBRIG and then every 2 weeks during the first 3 months of treatment. Thereafter, monitoring should be performed periodically. Based on the severity of the laboratory abnormalities, treatment should be withheld, and the dose modified. Hyperglycaemia: Fasting serum glucose should be assessed prior to initiation of ALUNBRIG and monitored periodically thereafter. Antihyperglycaemic medications should be initiated or optimised as needed. If adequate hyperglycaemic control cannot be achieved with optimal medical management, ALUNBRIG should be withheld until adequate hyperglycaemic control is achieved; upon recovery, dose reduce ALUNBRIG as per the SmPC or permanent discontinuation may be considered. Photosensitivity and photodermatosis: Photosensitivity to sunlight has occurred in patients treated with ALUNBRIG. Patients should be advised to avoid prolonged sun exposure while taking ALUNBRIG and for at least 5 days after discontinuation of treatment. When outdoors, advise patients to wear a hat and protective clothing and to use a broad-spectrum Ultraviolet A/B sunscreen and lip balm (SPF≥30). For severe photosensitivity reactions (≥Grade 3) withhold ALUNBRIG until recovery to baseline. The dose should be modified accordingly. Lactose: ALUNBRIG contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption should not take ALUNBRIG. Sodium: ALUNBRIG is essentially 'sodium-free' containing less than 1 mmol sodium (23 mg) per tablet. **Interactions:** Avoid use with strong CYP3A inhibitors. Avoid use with strong and moderate CYP3A inducers. Please refer to SmPC for further information and guidance for situations where use cannot be avoided. Grapefruit or grapefruit juice should be avoided. Coadministration of ALUNBRIG with CYP3A substrates with a narrow therapeutic index should be avoided as ALUNBRIG may reduce their effectiveness. Co-administration of ALUNBRIG with substrates of P-glycoprotein, breast cancer resistance protein, organic cation transporter 1, multidrug and toxin extrusion protein (MATE) 1 and 2K may increase their plasma concentrations. Patients should be closely monitored when ALUNBRIG is co-administered with substrates of these transporters with a narrow therapeutic index. **Fertility, pregnancy and lactation:** Women of reproductive potential should be advised not to become pregnant and to use effective non-hormonal contraception during treatment with ALUNBRIG and for at least 4 months following the final dose. Men should be advised not to father a child during ALUNBRIG treatment. Men with female partners of reproductive potential should be advised to use effective contraception during and for at least 3 months after the last ALUNBRIG treatment. No clinical data on the use of ALUNBRIG in pregnant women. ALUNBRIG should not be used during pregnancy unless the clinical condition of the mother requires treatment. Breast-feeding should be stopped during treatment with ALUNBRIG. No human data are available on the effect of ALUNBRIG on fertility. **Undesirable effects:** Very common (≥1/10): Pneumonia, upper respiratory tract infection, anaemia, lymphocyte count decreased, APTT increased, white blood cell count decreased, neutrophil count decreased, hyperglycaemia, hyperinsulinaemia, hypophosphataemia, hypomagnesaemia, hypercalcaemia, hyponatraemia, hypokalaemia, decreased appetite, headache, peripheral neuropathy, dizziness, visual disturbance, hypertension, cough, dyspnoea, lipase increased, diarrhoea, amylase increased, nausea, vomiting, abdominal pain, constipation, stomatitis, AST increased, ALT increased, alkaline phosphatase increased, rash, pruritus, blood CPK increased, myalgia, arthralgia, blood creatinine increased, fatigue, oedema, pyrexia. Common (≥1/100 to <1/10): Decreased platelet count, insomnia, memory impairment, dysgeusia, bradycardia, electrocardiogram QT prolonged, tachycardia, palpitations, pneumonitis, dry mouth, dyspepsia, flatulence, blood lactate dehydrogenase increased, hyperbilirubinaemia, dry skin, photosensitivity reaction, musculoskeletal chest pain, pain in extremity, musculoskeletal stiffness, non-cardiac chest pain, chest discomfort, pain, blood cholesterol increased, weight decreased. Other serious undesirable effects: Uncommon: (≥1/1,000 to <1/100): Pancreatitis. **Refer to the SmPC for details on full side effect profile and interactions. Legal classification**: POM. **Marketing authorisation (MA) numbers:** EU/1/18/1264/011, EU/1/18/1264/008, EU/1/18/1264/010, EU/1/18/1264/012. **Name and address of MA holder:** Takeda Pharma A/S, Delta Park 45, 2665 Vallensbaek Strand, Denmark. Additional information is available on request at: medinfoemea@takeda.com. **PI approval code:** pi-01842. **Date of Preparation:** January 2022.

▼This medicinal product is subject to additional monitoring. Adverse Events should be reported to the Pharmacovigilance Unit at the Health Products Regulatory Authority. Reporting forms and information can be found at: www.hpra.ie. Adverse events should also be reported to Takeda at: AE.GBR-IRL@takeda.com