

Refer to the Summary of Product Characteristics (SmPC) before prescribing.

Presentation: Brigatinib 180 mg, 90 mg and 30 mg film-coated tablets.

Indication: As monotherapy for the treatment of adult patients with anaplastic lymphoma kinase-positive advanced non-small cell lung cancer previously treated with crizotinib. **Dosage & 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. See SmPC for full dosage information and dose modifications. **Paediatric populations:** No data are available. **Elderly patients:** Dose adjustment is not required in elderly patients. 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.). **Contraindications:** Hypersensitivity to the active substance or to any of the excipients.

Warnings and Precautions: See SmPC for recommended dose modifications. **Pulmonary adverse reactions:** Patients should be monitored for new or worsening respiratory symptoms (e.g., dyspnoea, cough, etc.), particularly in the first week of treatment. If 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. Withhold Alunbrig in patients with severe hypertension (\geq 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, 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 AST, 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; **Lactose:** Alunbrig contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption should not take Alunbrig. **Interactions:** Avoid use with strong CYP3A inhibitors. See SmPC for dosage modifications for Alunbrig if concomitant use with a strong CYP3A inhibitor cannot be avoided. Strong and moderate CYP3A inducers should be avoided. Grapefruit or grapefruit juice should be avoided. Co-administration 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-gp, BCRP, 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 ($\geq 1/10$):** Pneumonia, upper respiratory tract infection, anaemia, lymphocyte count decreased, APTT increased, white blood cell count decreased, neutrophil count decreased, decreased platelet count, hyperglycaemia, hyperinsulinaemia, hypophosphataemia, decreased appetite, hypokalaemia, hypomagnesaemia, hyponatraemia, hypercalcaemia, insomnia, headache, peripheral neuropathy, dizziness, visual disturbance, hypertension, cough, dyspnoea, lipase increased, nausea, diarrhoea, amylase increased, vomiting, constipation, abdominal pain, dry mouth, stomatitis, AST increased, ALT increased, alkaline phosphatase increased, rash, pruritus, blood CPK increased, myalgia, arthralgia, musculoskeletal chest pain, blood creatinine increased, fatigue, oedema, pyrexia. **Common ($\geq 1/100$ to $< 1/10$):** Memory impairment, dysgeusia, tachycardia, electrocardiogram QT prolonged, bradycardia, palpitations, pneumonitis, dyspepsia, flatulence, blood lactate dehydrogenase increased, hyperbilirubinaemia, dry skin, photosensitivity reaction, pain in extremity, musculoskeletal stiffness, pain, non-cardiac chest pain, chest discomfort, weight decreased. **Other serious uncommon ($\geq 1/1,000$ to $< 1/100$) undesirable effects:** pancreatitis. **Refer to the SmPC for details on full side effect profile and interactions. Legal Classification:** POM. **UK Basic NHS Price:** 30mg x56: £2,450, 30mg x 28: £1,225, 90mg tablets x 28: £3,675, 90mg tablets x 7: £918.75, 180mg tablets x 28: £4,900, Alunbrig treatment initiation pack: £4,900 **Marketing Authorisation Numbers:** EU/1/18/1264/003, EU/1/18/1264/011, EU/1/18/1264/008, EU/1/18/1264/007, EU/1/18/1264/010, EU/1/18/1264/012 **Additional information is available on request from:** Takeda UK Ltd. Building 3, Glory Park, Glory Park Avenue, Wooburn Green, Buckinghamshire, HP10 0DF. Tel: 01628 537900 Fax: 01628 526617. Takeda Products Ireland Ltd. 3013 Lake Drive, Citywest Business Campus, Dublin 24. Tel: +353 (0)1 642 0021 Fax: +353 (0)1 642 0020 are responsible for the sale of ALUNBRIG in Ireland. ALUNBRIG® is a registered trademark. **PI Approval Code:** UK/BRIG/1903/0023 **PI Date of Preparation:** April 2019

UK: Adverse events should be reported to the Medicines and Healthcare products Regulatory Agency.

Reporting forms and information can be found at <https://yellowcard.mhra.gov.uk/>. Adverse events should also be reported to Takeda UK Ltd 01628 537900

Ireland: Adverse Events should be reported to the Pharmacovigilance Unit at the Health Products Regulatory Authority (medsafety@hpra.ie).

Information about Adverse Event reporting can be found on the HPRAs website (www.hpra.ie). Adverse events should also be reported to Takeda UK Ltd 1800 937 970