Prescribing Information (UK)

GIOTRIF® (afatinib)
Tablets containing 20, 30, 40 or 50 mg afatinib (as dimaleate). **Indication:** GIOTRIF as monotherapy is indicated for the treatment of: (i) Epidermal Growth Factor Receptor (EGFR) tyrosine kinase inhibitor (TKI)-naïve adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating EGFR mutation(s); (ii) Adult patients with locally advanced or metastatic NSCLC of squamous histology progressing on or after platinum-based chemotherapy. **Dose and Administration:** 40 mg once daily. Dose escalation to a maximum of 50 mg/day may be considered in patients who tolerate a 40 mg/day starting dose (i.e. absence of diarrhoea, skin rash, stomatitis, and other adverse reactions with CTCAE Grade > 1) in the first cycle of treatment. Symptomatic adverse reactions (e.g. severe/persistent diarrhoea or skin related adverse reactions) may be successfully managed by treatment interruption and dose reductions or treatment discontinuation. See SPC for further information on dosage. If interstitial lung disease (ILD) is suspected treatment should be interrupted pending evaluation. If ILD is diagnosed, GIOTRIF should be discontinued. P-glycoprotein (P-gp) inhibitors should be taken 6 hours apart (if dosed twice daily) or 12 hours apart (if dosed once daily) from GIOTRIF. Mild (estimated glomerular filtration rate (eGFR) 60-89 mL/min/1.73m²), moderate (eGFR 30-59 mL/min/1.73m²) or severe (eGFR 15-29 mL/min/1.73m²) renal impairment: no adjustment to starting dose necessary. Monitor patients with severe renal impairment (eGFR 15-29 mL/min/1.73m²) and adjust dose if not tolerated. Not recommended in patients with eGFR < 15 mL/min/1.73m² or on dialysis. Mild or moderate hepatic impairment: no adjustment to starting dose necessary. Not recommended in patients with severe hepatic impairment. Treatment of children or adolescents is not recommended. Tablets should be swallowed whole with water or dispersed in water and consumed immediately. Tablets should be taken without food. Food should not be consumed for at least 3 hours before and at least 1 hour after taking GIOTRIF.
Contraindications: Hypersensitivity to afatinib or to any of the excipients.
Warnings and Precautions: Diarrhoea, including severe diarrhoea, has been reported most frequently within the first 6 weeks of treatment. Diarrhoea may result in dehydration, in rare cases with fatal outcome. Anti-diarrhoeal medicinal products should be readily available so that treatment can be initiated at first signs of diarrhoea. Severe diarrhoea may require interruption and dose reduction or discontinuation of therapy. Rash/acne has been reported which may occur or worsen in areas exposed to the sun. Severe skin reactions may require temporary interruption of therapy, dose reduction, additional therapeutic intervention and referral to a specialist. Treatment should be interrupted or discontinued if the patient develops severe bullous, blistering or exfoliating conditions. Closer monitoring in female patients, patients with lower body weight and those with underlying renal impairment is recommended. There have been reports of ILD or ILD-like adverse reactions, including fatalities, in patients receiving GIOTRIF for treatment of NSCLC. Treatment should be interrupted if ILD is suspected. If ILD is diagnosed GIOTRIF should be permanently discontinued and appropriate treatment initiated. Hepatic failure, including fatalities, has been reported during treatment in less than 1% of patients. Periodic liver function testing is recommended in patients with pre-existing liver disease. Worsening of liver function: dose interruption may become necessary. If severe hepatic impairment develops, treatment should be discontinued. Gastrointestinal perforation, including fatalities, has been reported during treatment with GIOTRIF in 0.2% of patients across all randomized controlled clinical trials. In the majority of cases, gastrointestinal perforation was associated with other known risk factors. In patients who develop

gastrointestinal perforation while taking GIOTRIF, treatment should be permanently discontinued. Acute or worsening eye inflammation, lacrimation, light sensitivity, blurred vision, eye pain and/or red eye may indicate keratitis or other eye pathology therefore refer promptly to an ophthalmology specialist. If ulcerative keratitis is confirmed, treatment should be interrupted or discontinued. Use with caution in patients with a history of keratitis, ulcerative keratitis or severe dry eye. Left ventricular dysfunction has been associated with HER2 inhibition. Cardiac risk factors, conditions that can affect left ventricular ejection fraction (LVEF) and those who develop cardiac signs/symptoms during treatment: cardiac monitoring including LVEF assessment should be considered. Ejection fraction below the institution's lower limit of normal: cardiac consultation and treatment interruption or discontinuation should be considered. Concomitant treatment with strong inducers of P-gp may decrease exposure to afatinib. Contains lactose. Patients with galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this product. **Interactions:** Administer strong P-gp inhibitors (e.g. ritonavir, cyclosporine A, ketoconazole, itraconazole, erythromycin, verapamil, quinidine, tacrolimus, nelfinavir, saquinavir, and amiodarone) using staggered dosing, preferably 6 hours or 12 hours apart from GIOTRIF. Strong P-gp inducers (e.g. rifampicin, carbamazepine, phenytoin, phenobarbital or St. John's wort *(Hypericum perforatum)*) may decrease exposure. Afatinib is a moderate inhibitor of P-gp. It is unlikely that treatment will result in changes of the plasma concentrations of other P-gp substrates. Afatinib may increase the bioavailability of orally administered breast cancer resistance protein (BCRP) substrates (e.g. rosuvastatin and sulfasalazine). **Fertility, pregnancy and lactation:** Women of childbearing potential should be advised to avoid becoming pregnant while receiving treatment with GIOTRIF. Adequate contraception should be used during therapy and for at least 1 month after the last dose. There are no or limited amount of data from the use in pregnant women. Mothers should be advised against breast-feeding while receiving this product. An adverse effect on human fertility cannot be excluded**. Undesirable effects:** The most frequent adverse drug reactions were diarrhoea and skin related adverse events as well as stomatitis and paronychia. ILD-like adverse reactions were reported in 0.7% of afatinib treated patients. Bullous, blistering and exfoliative skin conditions have been reported including rare cases suggestive of Stevens-Johnson syndrome and toxic epidermal necrolysis although in these cases there were potential alternative aetiologies. Very common (≥1/10): paronychia, decreased appetite, epistaxis, diarrhoea, stomatitis, nausea, vomiting, rash, dermatitis acneiform, pruritus, dry skin. Common (≥1/100 to ≤1/10): cystitis, dehydration, hypokalaemia, dysgeusia, conjunctivitis, dry eye, rhinorrhoea, dyspepsia, cheilitis, alanine aminotransferase increased, aspartate aminotransferase increased, palmar-plantar erythrodysaesthesia syndrome, nail disorders, muscle spasms, renal impairment/renal failure, pyrexia, weight decreased. Uncommon (≥1/1,000 to < 1/100): Keratitis, interstitial lung disease, pancreatitis, gastrointestinal perforation. Rare (≥1/10,000 to <1/1,000): Stevens-Johnson syndrome, toxic epidermal necrolysis. Prescribers should consult the Summary of Product Characteristics for further information on side effects. **Pack sizes and NHS price:** *20 mg* 28 tablets £2023.28; 30 mg 28 tablets £2023.28*; 40 mg* 28 tablets £2023.28; *50 mg* 28 tablets £2023.28 **Legal category:** POM **MA numbers:** *20 mg* EU/1/13/879/003 (28 x 1 film-coated tablets); *30 mg* EU/1/13/879/006 (28 x 1 film-coated tablets); *40 mg* EU/1/13/879/009 (28 x 1 film-coated tablets); *50 mg* EU/1/13/879/012 (28 x 1 film-coated tablets) **Marketing Authorisation Holder:** Boehringer Ingelheim International GmbH, Binger Strasse 173, D-55216 Ingelheim am Rhein, Germany. Prescribers should consult the Summary of Product Characteristics for full prescribing information. **Prepared in January 2020.**

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Boehringer Ingelheim Drug Safety on 0800 328 1627 (freephone).