Indication	• Adjuvant treatment of stage IB-IIIA or N2 only stage IIIB (T3 N2 or T4 N2) NSCLC whose tumours have either an EGFR exon 19 deletion or exon 21 (L858R) substitution mutation after complete tumour resection. NB: Treatment to start no more than 10 weeks after surgery if no adjuvant chemotherapy, OR no more than 26 weeks after surgery, if patient received adjuvant chemotherapy. The patient must have had no prior treatment with an EGFR inhibitor or any other pre-operative systemic therapy (cytotoxic chemotherapy, immunotherapy) for the NSCLC. • First line treatment of locally advanced or metastatic EGFR receptor mutation-positive non-small cell lung cancer. NB the patient must have not had prior treatment with an EGFR inhibitor unless afatinib or dacomitinib or erlotinib or gefitinib has had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression or osimertinib has been received via Interim NHS England COVID19 funding or osimertinib has been received as part of an AstraZeneca compassionate use scheme. • Second-line treatment of adult patients with locally advanced or metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive NSCLC which has progressed after treatment with an EGFR TKI.
Treatment Intent	Palliative Adjuvant
Frequency and number of cycles	Repeat every 28 days. Palliative: Continuous until disease progression or unacceptable toxicity or patient choice. Adjuvant: Continuous until disease progression or unacceptable toxicity or patient choice or for a total treatment duration of 3 calendar years. NB a formal medical review must be scheduled to take place by the end of the second cycle to review tolerance and whether to continue treatment.
Monitoring Parameters pre-treatment	• Monitor FBC, LFTs & U&Es at each cycle. • If neuts <1.0 or PLTs <50 interrupt treatment until recovered. If counts recover within 3 weeks of stopping osimertinib, re-start treatment either at 80mg od, or with a reduction to 40mg od. If blood counts do not recover after 3 weeks, permanently discontinue. • For patients with CHF, electrolyte abnormalities or taking medication known to prolong QTc, monitor electrolytes and ECGs at baseline, after one month then as clinically indicated. Refer to Table 1 for dose modifications. • Cardiac monitoring including an assessment of LVEF at baseline and during treatment, should be considered in patients with cardiac risk factors, conditions that can affect LVEF, and in patients who develop relevant cardiac signs/symptoms during treatment. • In adjuvant therapy it should be confirmed the patient does not have brain metastases either by CT or MR imaging of the brain performed either before surgery or prior to starting osimertinib. • **Hepatic impairment:** No dose adjustments recommended in mild or moderate (Child Pugh A or B) hepatic impairment. No dose adjustment is recommended if

	bilirubin ≤ 3 x ULN and any AST or total bilirubin ≤ ULN and AST >ULN. The safety and efficacy has not been established in severe hepatic impairment and is therefore not recommended. • **Renal impairment:** No dose adjustment in mild, moderate or severe renal impairment. Limited data is available, and as such, caution is recommended in patients with end stage renal impairment (CrCl <15ml/min). • **Dose Modification:** Dosing interruption and/or dose reduction may be required based on individual safety and tolerability. If dose reduction is necessary, then the dose should be reduced to 40 mg taken once daily. • **Management of adverse reactions and dose adjustments:** • Refer to Table 1 for dose modifications in the event of adverse reactions. • Assessment of all patients with an acute onset and/or unexplained worsening of pulmonary symptoms (dyspnoea, cough, fever) should be performed to exclude ILD. Treatment should be suspended whilst symptoms are investigated. If ILD or pneumonitis is confirmed – permanently discontinue osimertinib • Steven Johnsons syndrome (SJS): Cases of SJS have been observed. If symptoms or signs of SJS appear, treatment with osimertinib should be interrupted or discontinued and the patient referred to a specialised unit for assessment and treatment. • Routine use of skin moisturiser should be encouraged. • **<u>Common drug interactions (for comprehensive list refer to BNF/SPC)</u>:** • Concomitant use of strong CYP3A inducers (e.g. rifampicin, carbamazepine, phenytoin,) should be avoided. Concomitant use of St John's wort is contraindicated. Moderate CYP3A4 inducers should be used with caution. • **Missed dose**: If a dose is missed, then it should be taken as soon as the patient remembers unless it is less than 12 hours before the next dose, in which case the patient should not take the missed dose. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet and Macmillan information sheet.
References	LUN-031 v2 SPC accessed online 01.12.21 Blueteq form accessed online 31.12.2021 CDF V1.197 accessed online 01.21.21

NB For funding information, refer to CDF and NICE Drugs Funding List

Table 1

Target organ	Adverse reaction	Dose modification
Pulmonary	ILD/Pneumonitis	Permanently discontinue
Cardiac	QTc interval greater than 500 msec on at least 2 separate ECGs	Withhold until QTc interval is less than 481 msec or recovery to baseline if baseline QTc is greater than or equal to 481 msec, then restart at a reduced dose (40 mg).
	QTc interval prolongation with signs/symptoms of serious arrhythmia	Permanently discontinue
Other, including: • Primary rash • Diarrhoea • Mucositis	Grade 3 or higher adverse reaction	Withhold osimertinib for up to 3 weeks
	If Grade 3 or higher adverse reaction improves to Grade 0-2 after withholding of TAGRISSO for up to 3 weeks	Osimertinib may be restarted at the same dose (80 mg) or a lower dose (40 mg)
	Grade 3 or higher adverse reaction that does not improve to Grade 0-2 after withholding for up to 3 weeks	Permanently discontinue.

Repeat every 28 days.

TTO	Drug	Dose	Route	Directions
Day 1	**OSIMERTINIB**	**80mg**	PO	OD. Available as 40mg and 80mg tablets. Swallow whole at the same time each day. Tablets should not be chewed or crushed. For patients who cannot swallow tablets, the dose may be dispersed in approx 50ml of noncarbonated drinking water. The tablet should be dropped into the water without crushing it, and stirred until dispersed. The dispersion should be swallowed immediately. The glass should then be rinsed with further water which should also be swallowed.
	Metoclopramide	10mg	PO	10mg TDS PRN. Do not take for more than 5 days continuously. (dispense 1x op on cycle 1, then only when required)
	Loperamide	2mg-4mg	PO	Take 4mg initially then 2mg after each loose stool when required (max 16mg a day) (dispense 1x op on cycle 1, then only when required)