Indication	Monotherapy for the treatment of EGFR wild type ROS1 and ALK negative advanced NSCLC harbouring mesenchymal-epithelial transition factor gene (MET) exon 14 (METex14) skipping alterations. NB the patient must not have been previously treated with a drug specifically targeting a MET exon 14 skipping alteration unless the patient received tepotinib via the EAMS program
Treatment Intent	Palliative
Frequency and number of cycles	Continuous therapy; repeat cycle every 28 days. Continue until disease progression, unacceptable toxicity or patient's choice. A formal medical review must be undertaken before the start of the second month to assess tolerability and before the third month of treatment to decide whether treatment should continue.
Monitoring Parameters pre-treatment	• Monitor FBC, LFTs and U&Es at baseline, every 2 weeks for the first three cycles of treatment then at each cycle thereafter. NB: Observed increases in creatinine may be the result of inhibition of active tubular secretion rather than renal injury. Renal function estimates that rely on serum creatinine (creatinine clearance or estimated glomerular filtration rate) should be interpreted with caution considering this effect. • The patient should either have no known brain metastases or if they do be symptomatically stable prior to starting treatment. • **Hepatic impairment:** No dose adjustment is recommended in patients with mild (Child Pugh Class A) or moderate (Child Pugh Class B) hepatic impairment. No data available in severe hepatic impairment (Child Pugh C), clinicians' decision. • **Renal impairment:** No dose adjustment is recommended in patients with mild or moderate renal impairment (CrCl 30 to 89 mL/min). No data available in severe renal impairment (<30ml/min), clinicians' decision. • **Dose Modification:** Dose interruption, dose reduction or discontinuation of treatment with tepotinib may be required based on adverse reactions. The recommended dose reduction is 225 mg daily. Tepotinib should be permanently discontinued if patients are unable to tolerate 225 mg. • **Management of adverse reactions and dose adjustments: (see table 1)** • Tepotinib has been associated with life-threatening ILD / pneumonitis. If patients present with new or worsening respiratory symptoms such as dyspnoea, cough and fever, or a radiological abnormality occurs, treatment should be interrupted and prompt investigation initiated. If interstitial lung disease/pneumonitis is confirmed, treatment should be permanently discontinued and the patient treated appropriately. • Oedema (peripheral, generalised and localised) has been reported as a very common adverse reaction, treatment interruption or dose adjustment may be required. • Increases in ALT and/or AST have been reported. If Grade 3 or higher increases in ALT/ AST occur, dose adjustment is recommended, see table below. • **<u>Common drug interactions (for comprehensive list refer to BNF/SPC)</u>:** • Concomitant use of strong CYP3A inducers (e.g. carbamazepine, phenytoin, phenobarbital, rifampicin), strong P-gp inducers and concomitant use of dual strong CYP3A and P-gp inhibitors (e.g. itraconazole) should be avoided • Monitoring of the clinical effects of P gp-dependent substances with a narrow therapeutic index (e.g. digoxin) is recommended during co-administration with tepotinib. • Tepotinib may have the potential to alter the exposure to co-administered metformin, monitoring of the clinical effects of metformin is recommended.

	• Tepotinib can inhibit the transport of sensitive substrates of the Breast Cancer Resistance Protein (BCRP). Monitoring of the clinical effects of sensitive BCRP substrates (e.g rosuvastatin, cimetidine, nitrofurantoin), is recommended during co-administration with tepotinib. • **Missed dose:** If a dose of tepotinib is missed, if more than 8 hours before the next dose it should be taken, if less than 8 hours the dose should be omitted and dosing should be resumed at the next scheduled dose. • If vomiting occurs after taking a dose advise the patient to take the next dose at the next scheduled time. • For oral self-administration: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet. • Patients should be advised that tepotinib may affect their ability to drive or operate machinery. • Contains Lactose.
References	SPC accessed online 20.04.2022 CDF list V1.210 accessed online 20.04.2022 CTCAE V5 accessed online 16.06.2022

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

Table 1

Adverse reaction	Severity	Dose Modification
Interstitial Lung Disease (ILD)	Any grade	Withhold tepotinib if ILD is suspected. Permanently discontinue if ILD is confirmed.
Increased ALT and/or AST without increased total bilirubin	Grade 3 >5.0 - 20.0 x ULN if baseline was normal; >5.0 - 20.0 x baseline if baseline was abnormal	Withhold until recovery to baseline ALT/AST. If recovered to baseline within 7 days, then resume at the same dose; otherwise resume at a reduced dose.
	Grade 4 >20.0 x ULN if baseline was normal; >20.0 x baseline if baseline was abnormal	Permanently discontinue
Increased ALT and/or AST with increased total bilirubin in the absence of cholestasis or haemolysis	ALT and/or AST greater than 3 times ULN with total bilirubin greater than 2 times ULN	Permanently discontinue
Increased total bilirubin without concurrent increased ALT and/or AST	Grade 3 >3.0 - 10.0 x ULN if baseline was normal; >3.0 - 10.0 x baseline if baseline was abnormal	Withhold until recovery to baseline bilirubin. If recovered to baseline within 7 days, then resume at a reduced dose; otherwise permanently discontinue.
	Grade 4 >10.0 x ULN if baseline was normal; >10.0 x baseline if baseline was abnormal	Permanently discontinue
Other adverse reactions	Grade 2	Maintain dose level. If intolerable, consider withholding tepotinib until resolved, then resume at a reduced dose.
	Grade 3	Withhold until resolved, then resume at a reduced dose.
	Grade 4	Permanently discontinue

Continuous
Repeat 28-day cycle

TTO	Drug	Dose	Route	Directions
Day 1	**TEPOTINIB**	**450mg**	PO	OD Swallow tablets whole with food. Do not chew, crush or split tablets. Available as 225mg tablets. Dispense 30 days supply
	Metoclopramide	10mg	PO	10mg up to three times a day PRN. Do not take for more than 5 days continuously. Dispense on Cycle 1 only, then only if required
	Loperamide	2mg	PO	Take two capsules (4mg) after first loose stool, then one capsule (2mg) after each loose stool when required. (Maximum 16mg per day). Dispense on Cycle 1 only, then only if required.