Mobocertinib (Lung)

Indication
Treatment of advanced or metastatic non-small cell lung cancer (NSCLC) that is positive for an EGFR exon 20 insertion mutation after platinum-based chemotherapy.

(NICE TA855)

ICD-10 codes
C34

Regimen details

Drug	Dose	Route
Mobocertinib	160mg OD	Oral

Cycle frequency
Continuous

Number of cycles
Until disease progression or unacceptable toxicity

Administration
Mobocertinib is available as 40mg capsules

Mobocertinib should be taken at approximately the same time each day and may be taken with or without food. The capsules should be swallowed whole. The capsules should not be opened, chewed or the contents dissolved.

Grapefruit or grapefruit juice should be avoided whilst taking mobocertinib.

If a dose is missed by more than 6 hours, the patient should not take the dose on that day but should resume the usual dosing on the following day at the regularly scheduled time. If a patient vomits after taking a dose, the patient should not repeat the dose but should resume the usual dosing as prescribed the following day.

The co-administration of mobocertinib with strong CYP3A4 inhibitors is **contraindicated**.

Pre-medication
Nil

Emetogenicity
This regimen has low emetic potential – refer to local policy

Additional supportive medication
It is recommended patients should have loperamide readily available when starting treatment and should take at the first episode of poorly formed or loose stools or the earliest onset of bowel movement more frequent than normal.

Extravasation

N/A

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U&E (including creatinine)*	14 days
LFTs	14 days
Magnesium*	14 days
Calcium*	14 days
Amylase/Lipase	14 days
Blood pressure	14 days
ECG (for QTc interval)	Baseline
Echocardiogram	Baseline

* Correct any electrolyte abnormalities prior to initiating treatment with mobocertinib

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	Monthly
U&E (including creatinine)	Monthly
LFTs	Monthly
Magnesium	Monthly
Potassium	Monthly
Amylase/Lipase	Monthly
Blood pressure	Monthly
ECG	Monthly for first 3-6 months then as clinically indicated
Echocardiogram	After 3-4 months then as clinically indicated

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	Limit
Neutrophils	≥ 1.0 x 10^9/L
Platelets	≥ 50 x 10^9/L
Haemoglobin	≥ 80g/L
Amylase/Lipase	≤ 2 x ULN
Bilirubin	< 1.5 x ULN
Creatinine clearance (CrCl)	≥ 30ml/min
QTc interval	≤ 480 msec
Ejection fraction	>50% and < 10% drop from baseline

Dose modifications

Dose level	Dose
Full dose	160mg OD
First dose reduction	120mg OD
Second dose reduction	80mg OD

- **Haematological toxicity**

Toxicity	Action
Neutrophils < 1.0 x 10^9/L Or Platelets < 50 x 10^9/L Or Haemoglobin (Hb) < 80g/L	Withhold mobocertinib until recovery Resume mobocertinib at same dose or next lower dose If Grade 4 toxicity (Neutrophils < 0.5 x 10^9/L, Platelets < 25 x 10^9/L) despite dose reductions consider permanent discontinuation of mobocertinib

- **Renal impairment**

No dose adjustment is recommended in mild or moderate renal impairment. Mobocertinib has not been studied in severe renal impairment (CrCl <30ml/min) and is not recommended.

- **Hepatic impairment**

No dose adjustment is required for mild hepatic impairment (bilirubin < ULN with ALT/AST > ULN or bilirubin < 1.5 x ULN with any ALT/AST). Mobocertinib has not been studied in moderate or severe hepatic impairment and is not recommended.

- **Other toxicities**

Toxicity	**Definition**	**Action/Dose adjustment**
QTc interval prolongation	Grade 2 (QTc interval 481-500 msec)	**First occurrence:** Withhold mobocertinib until QTc interval ≤480 msec Upon recovery resume mobocertinib at the same dose **Recurrence:** Withhold mobocertinib until QTc interval ≤480 msec Upon recovery resume mobocertinib at the next lower dose or consider permanent discontinuation
	Grade 3 (QTc interval ≥ 501 msec or QTc interval > 60msec increase from baseline)	**First occurrence:** Withhold mobocertinib until QTc interval ≤480 msec Upon recovery resume mobocertinib at the next lower dose or consider permanent discontinuation **Recurrence:** Permanently discontinue mobocertinib
	Grade 4 (Torsade de Pointes; polymorphic ventricular tachycardia; signs/symptoms of severe arrhythmia)	Permanently discontinue mobocertinib
Decreased ejection fraction or heart failure	LVEF reduced to 40-50% or drop of 10-19% points from baseline	Withhold mobocertinib until LVEF >50% or baseline If recovered within 2 weeks restart mobocertinib at same dose or next lower dose If not recovered to baseline within 2 weeks, permanently discontinue mobocertinib.
	LVEF < 40% or ≥ 20% point drop from baseline or symptomatic heart failure	Permanently discontinue mobocertinib
Interstitial lung disease (ILD)/Pneumonitis	Any grade	Withhold mobocertinib if ILD/pneumonitis is suspected Permanently discontinue mobocertinib if ILD/pneumonitis is confirmed

Toxicity	Definition	Action/Dose adjustment
Diarrhoea	Grade 1 or first occurrence of Grade 2	No dose modification required. Initiate treatment with loperamide at first onset of diarrhoea.
	Intolerable or recurrent Grade 2 or Grade 3	Withhold mobocertinib until recovery to ≤ Grade 1. Resume mobocertinib at the same dose or next lower dose.
	Grade 4	**First occurrence:** Withhold mobocertinib until recovery to ≤ Grade 1. If recovered within 2 weeks, resume mobocertinib at next lower dose. If not recovered to ≤ Grade 1 within 2 weeks permanently discontinue mobocertinib **Recurrence:** Permanently discontinue mobocertinib
Amylase/lipase elevation	Grade 2 (2-5 x ULN and asymptomatic)	Continue mobocertinib at same dose or next lower dose
	Asymptomatic Grade 3 (> 5 x ULN)	Withhold mobocertinib until recovery to ≤Grade 1 (<2 x ULN). If recovered within 2 weeks, resume mobocertinib at same dose or next lower dose If not recovered to ≤Grade 1 within 2 weeks, permanently discontinue mobocertinib
	Symptomatic Grade 3 and Grade 4	Withhold mobocertinib until recovery to ≤Grade 1 (<2 x ULN). If recovered within 2 weeks, resume mobocertinib at the next lower dose If not recovered to ≤Grade 1 within 2 weeks, permanently discontinue mobocertinib
Other non-haematological toxicity	Grade 2	No dose modification is required. For intolerable or recurrent Grade 2 toxicity, withhold mobocertinib until symptoms resolve and resume mobocertinib at the same dose or the next lower dose
	Grade 3 or 4	Withhold mobocertinib until recovery to Grade 1 or lower; then resume mobocertinib at the same dose or the next lower dose. For Grade 4 toxicity, consider permanent discontinuation of mobocertinib.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
QT prolongation
Pneumonitis, interstitial lung disease
Cardiac failure

- **Frequently occurring side effects**

Diarrhoea
Rash, dry skin
Anaemia

Creatinine increased
Nausea, vomiting
Stomatitis
Amylase/Lipase increased
Anorexia
Paronychia
Fatigue
Hypomagnesaemia
Hypokalaemia
Hyponatraemia
Raised transaminases
Hypertension
Alopecia

- **Other side effects**

Dyspnoea
Palmar-plantar erythema

Significant drug interactions – for full details consult product literature/ reference texts

Strong CYP3A4 inhibitors (e.g. itraconazole, ritonavir, clarithromycin): co-administration is contraindicated due to increase in mobocertinib plasma concentrations.
M**oderate CYP3A4 inhibitors (e.g. fluconazole, erythromycin):** co-administration should be avoided. If co-administration of mobocertinib with a moderate CYP3A4 inhibitor is unavoidable, the dose of mobocertinib should be reduced by approximately 50% and increased frequency of QTc interval monitoring considered.
CYP3A4 inducers (e.g. rifampicin, carbamazepine, phenytoin, St John's wort): co-administration should be avoided due to reduced mobocertinib plasma concentrations
CYP3A substrates (e.g. midazolam, hormonal contraceptives): mobocertinib may reduce plasma concentrations of co-administered CYP3A substrates potentially leading to loss of efficacy.
P-gp (e.g. digoxin, dabigatran) and BCRP (e.g. sulfasalazine) substrates: mobocertinib may increase exposure to these substrates, use with caution and monitor for toxicity from the substrate.

Additional comments

Women of childbearing potential should be advised to use highly effective non-hormonal contraception during treatment with mobocertinib and for 1 month following the final dose. Men with female partners of childbearing potential should be advised to use effective contraception during treatment with mobocertinib and for 1 week following the final dose of mobocertinib.

References

- National Institute for Health and Care Excellence (NICE TA855) accessed 31st August 2023 via www.nice.org.uk
- Summary of Product Characteristics – Mobocertinib (EXKIVITY) accessed 31st August 2023 via www.medicines.org.uk
- Zhou, C. et al. Treatment Outcomes and Safety of Mobocertinib in Platinum-Pretreated Patients with EGFR Exon 20 Insertion-Positive Metastatic Non-Small Cell Lung Cancer: A Phase 1/2 Open-label nonrandomized clinical trial. JAMA Oncol. 2021;7(12):e214761

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