Tepotinib Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
As monotherapy for the treatment of adult patients with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14) skipping, who require systemic therapy following prior treatment with immunotherapy and/or platinum-based chemotherapy.	C34	00823a	ODMS 01/08/2024

* This is for post 2012 indications only.

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Tepotinib is administered orally once daily and should continue as long as clinical benefit is observed.

Drug	Dose	Route	Cycle
Tepotinib	450mg daily	PO with food	Continuous
The tablets should be taken with food and should be swallowed whole to ensure that the full dose is administered.			
If a daily dose is missed, it can be taken as soon as remembered on the same day, unless the next dose is due within 8 hours.			

ELIGIBILITY:

- Indication as above
- ≥18 years
- ECOG 0-2
- METex14 skipping mutation as confirmed by validated test method
- No EGFR activating mutation or ALK rearrangement

EXCLUSIONS:

- Hypersensitivity to tepotinib or any of the excipients
- Active CNS metastases
- Pregnancy
- Breast feeding

PRESCRIPTIVE AUTHORITY:

- The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:

Baseline tests:

- FBC, electrolytes, renal and liver profile
- ECG as clinically indicated
- Pregnancy test in women of childbearing potential

Regular tests:

- FBC, electrolytes, renal and liver profile
- ECG as clinically indicated
- Pregnancy test in women of childbearing potential, as clinically indicated

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant
- The recommended dose reduction level for the management of adverse reactions is 225 mg daily
- Detailed recommendations for dose modification for adverse events are provided in table 2 below

Renal and Hepatic Impairment:

Table 1: Dose Modification of Tepotinib in Renal and Hepatic Impairment

Renal Impairment		**Hepatic Impairment**	
CrCl (mL/min)	**Dose**	Child-Pugh A/B (or mild to moderate)	No dose adjustment is needed
≥30	No dose adjustment is needed	Child-Pugh C (or severe)	Not recommended
<30	No need for dose adjustment is expected		
Haemodialysis	No need for dose adjustment is expected		
Renal and hepatic: Giraud et al, 2023			

Management of adverse events:

Table 2: Dose Modifications of Tepotinib for Adverse Events

Adverse reactions	Severity	Recommended dose modification
Interstitial lung disease (ILD)	Any grade	Withhold treatment if ILD is suspected. Permanently discontinue treatment if ILD is confirmed.
Increased ALT and/or AST without increased total bilirubin	ALT and/or AST greater than 5 times up to 20 times ULN	Withhold treatment until recovery to baseline ALT/AST. If recovered to baseline within 7 days, then resume treatment at the same dose; otherwise resume treatment at a reduced dose.
	ALT and/or AST greater than 20 times ULN	Permanently discontinue treatment.
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 treatment.
Other adverse reactions	Grade 3 or higher	Reduce treatment to 225 mg until the adverse reaction recovers to ≤ grade 2. A temporary interruption of treatment for no more than 21 days can also be considered.

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic AntiCancer Therapy (SACT) Induced Nausea and Vomiting linked here

Minimal to low (**Refer to local policy).**

For information:
Within NCIS regimens, antiemetics have been standardised by the Medical Oncologists and Haemato-oncologists and information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - link here
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - link here

PREMEDICATIONS:

- No specific recommendations

OTHER SUPPORTIVE CARE:

- Treatment with anti-diarrhoeal agents, such as loperamide (4mg at first onset followed by 2mg after each loose stool (max 16 mg /day) or see local policy) should be started at the first sign of loose stools.
- Women of childbearing potential should use effective contraception during treatment and for at least 1 week after the last dose. Women using systemically acting hormonal contraceptives should add a barrier method during treatment and for at least 1 week after the last dose. Male patients with female partners of childbearing potential should use barrier contraception during treatment and for at least 1 week after the last dose.

ADVERSE EFFECTS:

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.
- **Tepotinib is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions.**

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

REFERENCES:

1. Paik P, et al. Tepotinib in Non-Small Cell Lung Cancer with MET Exon 14 Skipping Mutations. N Engl J Med 2020; 383:931-943.
2. Giraud EL, de Lijster B, Krens SD, Desar IME, Boerrigter E, van Erp NP. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Lancet Oncol 2023; 24: e229.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Antiemesis Version 1.2024 – December 13, 2023. Accessed June 2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf
4. Herrstedt J et al. 2023 MASCC and ESMO guideline update for the prevention of chemotherapy and radiotherapy induced nausea and vomiting. ESMO Open. 2024;9(2):102195. Accessed June 2024. Available at https://www.esmo.org/guidelines/guidelines-by-topic/esmo-clinical-practice-guidelines-supportive-and-palliative-care/prevention-of-chemotherapy-and-radiotherapy-induced-nausea-and-vomiting
5. Tepotinib (Tepmetko®) summary of Product Characteristics. Accessed June 2024. Available at https://www.ema.europa.eu/en/documents/product-information/tepmetko-epar-product-information_en.pdfdocument-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf

Version	Date	Amendment	Approved By
1	19/07/2024		Prof Maccon Keane
1a	01/08/2024	Reimbursement status updated	NCCP

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.