National Cancer Control Programme

NCCP Technology Review Committee (TRC)

Meeting Notes

Date of Meeting:	**25th March 2024 at 4.30pm**
Venue:	**Teleconference**
Assessment:	Tepotinib (Tepmetko®)

TEXT FOR REDACTION DUE TO DELIBERATIVE PROCESS HIGHLIGHTED IN YELLOW

TEXT FOR REDACTION DUE TO COMMERCIAL SENSITIVITY IS HIGHLIGHTED IN PINK

TEXT FOR REDACTION DUE TO CONFIDENTIALITY IS HIGHLIGHTED IN BLUE

Attendance:

Members present		
NCPE representative	National Centre for Pharmacoeconomics (NCPE)	By 'phone
Dr Dearbhaile Collins	Consultant Medical Oncologist, Cork University Hospital: ISMO nominee **(Chair)**	By 'phone
Dr Patrick Hayden	Consultant Haematologist, St James's :IHS representative	By 'phone
Ms Fiona Mulligan	PCRS representative	By 'phone
Prof Michael O'Dwyer	Consultant Haematologist, Galway :IHS representative	By 'phone
Dr Susan Spillane	HTA Directorate: HIQA nominee	By 'phone
Non-member invited specialists present		
Dr Jane Sui	Consultant Medical Oncologist	By 'phone
Apologies (members)		
Dr Neil Barrett	Consultant Haematologist, Children's Health Ireland - Crumlin	
Dr Oscar Breathnach	Medical Oncologist, Beaumont: ISMO nominee	
Dr Dearbhaile O'Donnell	Medical Oncologist, St. James's Hospital: ISMO nominee	
Observers present		
Ms Helena Desmond	Senior Pharmacist, NCCP	By 'phone
Ms Clare Meaney	Chief II Pharmacist, NCCP	By 'phone

Item	Discussion	Actions

1	**Introduction & reminder re. conflict of interest & confidentiality**	
	Members were reminded to raise any conflicts of interest that they had in relation to any drug for discussion prior to the commencement of the discussion of that item.	
2	**Notes of previous meeting and matters arising**	
	The notes of the previous meeting on February 26th were agreed.	
3	**Drugs/Technologies for consideration**	
	Tepotinib (Tepmetko®) (Ref. TRC 151) *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.* The clinical aspects of this indication were discussed, noting up to 50% of patients with NSCLC have an oncogenic driver, of this, *METex14* skipping mutation occurs in approximately 3-4% of patients globally and is associated with a significantly older age. In the Irish context, the incidence is reported as 2.6% (*Keogh et al* [1]). Currently, two drugs are licensed by the EMA for use in NSCLC which target the *METex14* skipping mutation, teponinib and capmatinib. It was noted that the reimbursement assessment for capmatinib will not be progressing. The supporting evidence for this indication is the VISION study, a phase II, single arm, open label study in patients with the METex14 skipping mutations. At the most recent data cut off (November 2022), the study showed an objective response rate (ORR) of 45% in patients treated with tepotinib in second and later lines. The median duration of response (DoR) was 12.6 months, progression free survival (PFS) was 11 months and median overall survival (OS) was 19.3 months. When compared to paclitaxel or docetaxel with or without nintedanib, ORRs for docetaxel with or without nintedanib ranges from 4-23%, PFS ranges from 3 to 4.5 months and OS with docetaxel ranges from 9 to 10.5 months. The safety profile of tepotininb was discussed, the most commons side effects associated with tepotinib are oedema ~77%, nausea 30%, hypoalbuminaemia 29% and diarrhoea 28%, as compared to chemotherapy where there are higher rates of haematological toxicities. Tepotinib also has intracranial activity, which is important as most patients with lung cancer will develop brain metastases. In general, tepotinib is a well-tolerated, oral treatment, taken once daily at home which may reduce the burden on the health care service. It was noted that after progression following chemotherapy, while there are a wide range of second line treatments, there is an unmet need for a *METex14* skipping targeted treatment, and there is a desire among the clinicians to have this treatment option available for this small patient cohort who tend to be older (≥70 years of age) and who currently do not have a targeted therapy available to them. The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed. The current standard of care (SOC) and relevant compactors were discussed. The supporting evidence was outlined, noting that the most recent data cut of November 2022 was not available for the NCPE assessment, therefore not included in the analysis. However the results are similar, ORR was 45% with a 95% confidence interval (CI) between 36.8- 53, 55% of patients had a PFS event, mPFS was 11 months, 61.1% had a OS event and mOS was 19.6 months based on the February data cut of 2022. The EMA considered that the ORR in the response durations were of a magnitude expected to provide a benefit to NSCLC patients with the *METex14* skipping mutation. The NCPE Review Group highlighted a number of limitations regarding the supporting evidence, such as the absence of a randomised comparison, the single arm and open label nature of the trial, small sample size and lack of direct comparator evidence. The cost	

[1] Keogh et al Genomic Landscape of NSCLC in the Republic of Ireland J Thoracic Oncol 2023; 5 (2): 100627

	effectiveness analysis was discussed. A number of adjustments to the model were made by the review group such as treatment duration and dose intensity. In terms of the cost, the cost for tepotinib per pack of 60 (225mg tablets) is €8,478 and total cost per treatment course is €116,270 (assuming 13.6 months of treatment based on the NCPE calculation of time to treatment discontinuation). In comparison, the cost of docetaxel is €1,569 per treatment course and docetaxel plus nintedanib is €18,731 per treatment course. In terms of the cost effectiveness analysis, for the Applicants base case analysis for the comparison with docetaxel plus nintedanib the ICERS was €108,461, and the ICER versus docetaxel is €78,648 per QALY. Changes were made in the NCPE-adjusted base case and NCPE-adjusted base case ICER versus docetaxel plus nintedanib was €239,257/ QALY and the ICER versus docetaxel is €152,045/QALY. There is 0% probability of cost effectiveness at either threshold when using the NCPE-adjusted base case. When compared to docetaxel a 78.4% reduction in price to wholesaler is required to achieve an ICER of €45,000/QALY and for docetaxel plus nintedanib a 75.97% reduction is required. In terms of the budget impact (BI), 9 patients are estimated to be eligible for treatment in year 1. The Applicant estimated the incidence *METex14* skipping mutation to be 2.2%, whereas the NCPE review group estimated a range of 3-4%, as opposed to the reported rate of 2.6% by *Keogh et al* among the Irish population, which significantly effects the BI model. Clinical opinion obtained indicated that *METex14* testing is part of SOC, however the Applicant's assumes a testing rate of 55% in year 1 rising to 90% in years 5, contradicting the assumption that all patients will be tested. The review group considered the estimated eligible population to be underestimated. Using the Applicant base case the the 5-year gross BI was estimated to be €4.29M and the net BI was estimated to be €4.04M. Using the NCPE-adjusted base case assumptions the 5-year gross BI was estimated to be €7.44M and the net BI estimated to be €7.04 M. When the proportion of eligible patients increases to 100% (i.e. assumed that 100% of patients will be tested), the [redacted]. The NCPE recommends that tepotinib not be considered for reimbursement unless cost-effectiveness can be improved relative to existing treatments. Having considered the clinical efficacy of the indication in this patient cohort there was a split vote where 3 committee members recommended the approval of this indication to the HSE Drugs Group subject to an improvement in cost, and 3 members recommended that this indication not be approved. *(Decision: TRC 151)*	
4	**Update on other drugs in the reimbursement process**	
	An update had been shared with the group in the documentation for the meeting	
5	**Next meeting**	
	The proposed date for the next meeting is April 22nd 2024	
6	**Any other business / Next meeting**	

The meeting concluded at 17.20pm.

Actions arising from meeting:

Ref.	Date of meeting	Details of action	Responsible	Update
24/01	25/03/2024	NCCP to communicate recommendations to HSE Drugs Group.	NCCP	Completed
24/01	25/03/2024	Apply for CPD	NCCP	Completed