National Cancer Control Programme

NCCP Technology Review Committee (TRC)

Meeting Notes

Date of Meeting:	**2nd October 2023 at 4.30pm**
Venue :	**Teleconference**
Assessment:	Enfortumab vedotin (Padcev®)
	Osimertinib (Tagrisso®)
	Atezolizumab (Tecentriq®)

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 Oscar Breathnach	Medical Oncologist, Beaumont: ISMO nominee	By 'phone
Dr Ronan Desmond	Consultant Haematologist, Tallaght University Hospital: IHS representative	By 'phone
Dr Michael Fay	Consultant Haematologist, Mater Hospital: IHS representative	By 'phone
Ms Patricia Heckmann	AND NCCP (Chair)	By 'phone
Ms Ellen McGrath	PCRS representative	By 'phone
Adrian Murphy	Medical Oncologist, Beaumont: ISMO nominee	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		
Apologies (members)		
Dr Dearbhaile Collins	Medical Oncologist, Cork University Hospital: ISMO nominee	
Dr Dearbhaile O'Donnell	Medical Oncologist, St. James's Hospital: ISMO nominee	
Observers present		
Ms Helena Desmond	Senior 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 September 4th 2023 were agreed.	
3	**Drugs/Technologies for consideration**	
	Osimertinib (Tagrisso®) **(Ref. TRC140)** *Adjuvant treatment after complete tumour resection in adult patients with stage IB-IIIA Non-Small Cell Lung Cancer (NSCLC) whose tumour has epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations.* The clinical aspects of this indication were discussed, noting that osimertinib is already in use for the treatment of NSCLC in the advanced setting for patients with an EGFR mutation. The supporting evidence for this indication is the phase III, randomised, double-blind, placebo-controlled ADAURA study which evaluated the safety and efficacy of osimertinib compared to placebo in patients with stage IB-IIIA EGFR-mutated NSCLC who have had complete tumour resection, with or without post-operative adjuvant chemotherapy. In terms of survival, the study showed a 5 year survival of 85% with osimertinib compared to 73% with placebo, a 12% gain in survival. With chemotherapy alone, a gain of only 5% is expected. The safety profile was discussed, and it was noted that clinicians are well used to using this agent in the advanced setting and in terms of toxicities these are well managed by the clinicians. Based on the enhanced 5 year survival, there is a strong desire among clinicians to have this treatment option available for this cohort of patients. The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed. The supporting evidence was outlined and the NCPE review group highlighted a number of limitations with the study, which included the statistical immaturity of the OS data, lack of validation between the relationship between the disease free survival (DFS) and OS and the early unplanned interim analysis. The cost effectiveness modelling was outlined, the limitations with the model were highlighted and adjustments made were noted. In terms of cost, treatment with osimertinib is associated with a cost of €216,000. The ICERS were outlined, in the Applicants base case, the ICER is €57,892 per QALY. A number of changes were made to the NCPE adjusted base case and the NCPE adjusted ICERS is €70,595 per QALY. In terms of budget impact (BI), the gross BI is estimated to be €16.43 million including VAT, over 5 years, and net BI is equivalent to the gross BI. [redacted] Having considered the clinical efficacy of the indication in this patient cohort the committee members agreed unanimously to recommend approval of this indication to the HSE Drugs Group One member was absence, but quorum in place *(Decision: TRC 140)*	

Enfortumab vedotin (Padcev®) **Ref. TRC 141**

As monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer (mUC) who have previously received a platinum-containing chemotherapy and a programmed death receptor-1 (PD-1) or programmed death-ligand 1 inhibitor (PD-L1).

The clinical aspects of this indication were discussed. The supporting evidence for this indication is the phase III, randomised trial – Study EV-301, which evaluated the safety and efficacy of enfortumab vedotin compared with single agent taxane (docetaxel, paclitaxel or vinflunine) chemotherapy in patients with locally advance or metastatic UC who had previously received a platinum-containing chemotherapy and a PD-1 or PD-L1 inhibitor. The primary endpoint was overall survival (OS) and after a median follow up of 11.1 months, the trial showed a 3.9 months absolute benefit favouring enfortumab vedotin, with an OS of 12.0 months in the enfortumab vedotin group vs 9 months in the chemotherapy group. Similarly in terms of the secondary endpoints, progression free survival (PFS), was 5.6 months in the enfortumab vedotin group vs 3.7 months in the chemotherapy group. With regards to overall response rates (ORR) enfortumab vedotin showed higher rates of complete and partial response with ~5 vs 2.7% and 35 vs 15.2% respectively. The safety profile was discussed, a number of safety concerns were highlighted such as neutropenia, rash, fatigue, neuropathy and anaemia, but it was noted that these are not too dissimilar to the current standard of care (SOC) taxane chemotherapy. There is desire among clinicians to have enfortumab vedotin available for this cohort of patients, who have limited treatment opinions.

The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed. The NCPE review group highlighted a number of limitations of the trial such as, open label nature of the trial, insufficient evidence to establish the clinical evidence in patients who receive avelumab as maintenance therapy, the early stopping of the trial and patient crossover. The cost effectiveness modelling was outlined and adjustments to the model were noted. In terms of the cost, treatment with enfortumab vedotin is assumed to be €63,122 including VAT and €50,525 excluding VAT. The average cost of chemotherapy is assumed to be [redacted]. In terms of cost effectiveness results for the applicant's base case the ICER was €161,060 per QALY, the NCPE review group adjusted a number of assumptions in the modelling, and the NCPE-adjusted base case the ICER was €195,334 per QALY. In both the applicants and the NCPE-adjusted base case there is a 0% probability of enfortumab vedotin being cost effective at both the €20,000 per QALY and €45,000 per QALY threshold and a total rebate of 81.7% would be required to being the ICER to below €45,000 per QALY with the NCPE-adjusted base case.

In terms of the budget impact (BI), the Applicant estimates that 41 patients will treated in year 1, increasing by 58 in year 5. The 5-year cumulative gross BI is estimated to be €16.22 million including VAT and €12.99 million excluding VAT. The 5-year cumulative net BI is estimated to be €13.93 million including VAT and €11.12 million excluding VAT. The recommendation of the NCPE review group was that enfortumab vedotin not be considered for reimbursement unless cost-effectiveness can be improved relative to existing treatments. This conclusion was reached due to the high level of uncertainty associated with the cost effectiveness analysis and the price reduction required. [redacted]

Having considered the clinical efficacy of the indication in this patient cohort the committee members agreed by a majority to recommend approval of this indication to the HSE Drugs Group.

	One member was absence, but quorum in place *(Decision: TRC 141)* Atezolizumab (Tecentriq®) **(Ref. TRC142)** *As adjuvant treatment following complete resection and platinum-based chemotherapy for adult patients with NSCLC with a high risk of recurrence whose tumours have PD-L1 expression on ≥ 50% of tumour cells (TC) and who do not have EGFR mutant or ALK-positive NSCLC.* Discussion of this item was deferred and will be added to the agenda for the next meeting.	
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 October 23rd 2023	
6	**Any other business / Next meeting**	

The meeting concluded at 5.25pm.

Actions arising from meeting:

Ref.	Date of meeting	Details of action	Responsible	Update
23/01	02/10/2023	NCCP to communicate recommendations to HSE Drugs Group.	NCCP	Complete
23/01	02/10/2023	Apply for CPD	NCCP	Complete
23/01	02/10/2023	Circulation of COI forms for 2023	NCCP	Complete