National Cancer Control Programme

NCCP Technology Review Committee (TRC)

Meeting Notes

Date of Meeting:	**31st March 2025 at 4.30pm**
Venue:	**Teleconference via MS Teams**
Assessment:	Lutetium (^{177}Lu) vipivotide tetraxetan (Pluvicto®)
	Tisagenlecleucel (Kymriah®)

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 MS Teams
Dr Neil Barrett	Consultant Haematologist, Children's Health Ireland – Crumlin **(Chair)**	By MS Teams
Dr Oscar Breathnach	Medical Oncologist, Beaumont: ISMO nominee	By MS Teams
Dr Dearbhaile O'Donnell	Medical Oncologist, St. James's Hospital: ISMO nominee	By MS Teams
Prof Michael O'Dwyer	Consultant Haematologist, Galway: IHS representative	By MS Teams
Dr Susan Spillane	HTA Directorate: HIQA nominee	By MS Teams
Louise Walsh	PCRS representative	By MS Teams
Non-member invited specialists present		
Dr Mathilde	NCCP National Medical Oncology Programme Clinical Advisor	By MS Teams
Apologies (members)		
Dr Dearbhaile Collins	Consultant Medical Oncologist, Cork University Hospital: ISMO nominee	
Dr Patrick Hayden	Consultant Haematologist, St James's: IHS representative	
Ms Aishling McLoughlin	Chief I Pharmacist, NCCP (Deputy Chair)	
Observers present		
Ms Elizabeth Breen	Chief II Pharmacist, NCCP	By MS Teams
Ms Helena Desmond	Senior Pharmacist, NCCP	By MS Teams

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 24th 2025 were reviewed and agreed.	
3	**Drugs/Technologies for consideration**	
	Lutetium (^{177}Lu) vipivotide tetraxetan (Pluvicto®) (**Ref. TRC 170)** *In combination with androgen deprivation therapy (ADT) with or without androgen receptor (AR) pathway inhibition for the treatment of adult patients with progressive prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with AR pathway inhibition and taxane-based chemotherapy.* The clinical aspects of this indication were discussed, lutetium (^{177}Lu) vipivotide tetraxetan is a radioligand therapy, an innovative therapy in oncology, and it was noted that lutetium (^{177}Lu) oxodotreotide is currently approved for the treatment of neuroendocrine tumours (NETs). The supporting evidence for this indication comes from the VISION trial, a randomised, open-label, phase III study which evaluated the use of lutetium^{177} vipivotide tetraxetan versus best standard of care (BSoC) in the treatment of adult patients with PSMA-positive mCRPC who had received prior treatment with AR pathway inhibition and taxane-based chemotherapy. Over 800 patients were randomly assigned, the primary efficacy endpoints were overall survival (OS) and radiographic progression-free survival (rPFS). Key secondary endpoints were overall response rate (ORR) and time to first symptomatic skeletal event (SSE). In term of the results, lutetium^{177} vipivotide tetraxetan plus BSoC significantly prolonged OS compared to BSoC alone. There was also a statistically significant increase in rPFS compared to BSoC alone and all key secondary endpoints also favoured the lutetium^{177} vipivotide tetraxetan plus BSoC group. It was acknowledged that in terms of OS, lutetium^{177} vipivotide tetraxetan may be comparable to the current treatments, highlighting the lack of comparative evidence with cabazitaxel a relevant comparator. However, it was highlighted that lutetium^{177} vipivotide tetraxetan would be an important treatment option for the subset of patients in this line of treatment who would be unfit to receive the current SOC, cabazitaxel, which is associated with significant toxicities. There is a desire among the clinicians to have this treatment option available to this patient cohort, noting that patient numbers would be small. It was also noted that lutetium^{177} vipivotide tetraxetan is currently recommended by international (NCCN) and European guidelines (ESMO) for this patient cohort. The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed. The current treatment pathway and relevant comparators were outlined. The supporting evidence was discussed. In terms of the median OS, there was a benefit seen with lutetium^{177} vipivotide tetraxetan, with a HR of 0.62, and with regard to the median PFS the HR WAS 0.44. The NCPE Review Group highlighted a number of limitations regarding the supporting evidence, such as palliative nature of the BSoC arm, a treatment that does not increase OS, the lack of direct comparative evidence with cabazitaxel, the most relevant comparator, and the high risk of bias due to the high number of withdrawals from the BSoC group for example. Due to the lack of comparative evidence, an indirect comparative analysis was conducted. A network meta-analysis (NMA) submitted by the Applicant was discussed, and the NCPE review group highlighted some concerns such as the heterogeneity of the study population leading to uncertainty with the clinical effectiveness estimates. An unanchored indirect comparison (ITC) was also conducted. Using the applicant NMA, lutetium^{177} vipivotide tetraxetan demonstrates statistically significant superior OS and PFS against androgen receptor pathway inhibitors (ARPIs) and cabazitaxel. For lutetium^{177} vipivotide tetraxetan against cabazitaxel the HR for OS is 0.6 and the HR for PFS is 0.4. The results of the	

NCPE alternative NMA did not find OS benefit for lutetium^{177} vipivotide tetraxetan, however there was still a statistically significant benefit for PFS. In the NCPE alternative NMA, the HR for OS is 0.99 and a confidence interval (CI) of 0.68-1.44, and the HR for PFS is 0.65. In the unanchored ITC for lutetium^{177} vipivotide tetraxetan versus cabazitaxel, a statistically significant benefit in OS was observed, however the HR point estimate was midway between the Applicants NMA and the NCPE alternative NMA result, with a HR of 0.76. Considering this, it is unclear if lutetium^{177} vipivotide tetraxetan is associated with an OS benefit over cabazitaxel. The cost effectiveness analysis and the modelling used was outlined. In terms of cost, the cost per treatment course of lutetium^{177} vipivotide tetraxetan is €102,000 including VAT, and €81,000 excluding VAT. The cost of cabazitaxel is [redacted]. In terms of the results, for the Applicant's base case for lutetium^{177} vipivotide tetraxetan versus BSoC the ICER is €202,452/QALY, versus cabazitaxel the ICER is €208,265/QALY. A number of changes were made to the NCPE base case. In the NCPE adjusted base case the ICER for lutetium^{177} vipivotide tetraxetan versus BSoC is €335,686/QALY, for lutetium^{177} vipivotide tetraxetan versus cabazitaxel (unanchored ITC) the ICER is €326,210/QALY, and for lutetium^{177} vipivotide tetraxetan versus cabazitaxel (NMA) the ICER is €1,338,064/QALY. The probability of cost effectiveness for both the Applicant and NCPE base cases is 0%. [redacted] using the cabazitaxel unanchored ITC to reach the willingness to pay threshold of €45,000 per QALY. In terms of the budget impact (BI), it is estimated that 15 patients will be treated in year 1 increasing to 84 in year 5. The net BI over 5 years is estimated to be €25.74 million including VAT and €20.57 million excluding VAT. The NCPE recommends that lutetium^{177} vipivotide tetraxetan not be considered for reimbursement.

Having considered the clinical efficacy of the indication in this patient cohort, after extensive deliberation, and considering the subset of patients who are unfit to receive the current SOC, cabazitaxel, the committee members agreed by majority to recommend approval of this indication to the HSE Drugs Group, subject to a significant improvement in cost.

(Decision: TRC 170)

Tisagenlecleucel (Kymriah®) (**Ref. TRC 171)**

For the treatment of adult patients with relapsed/refractory follicular lymphoma after 2 or more lines of therapy.

The clinical aspects of this indication were discussed, follicular lymphoma (FL) is a disease with relapsing/remitting course, and poor prognosis is associated where there are short intervals between treatment and progression representing an area in unmet need, particularly for patients who progress with 24 months of initial chemo-immunotherapy. It was noted that tisagenlecleucel is currently approved for reimbursement for the treatment of B-cell acute lymphoblastic leukaemia (ALL) and diffuse large B-cell lymphoma (DLBCL). The supporting evidence for this indication is the ELARA study, a phase II, single arm, open-label study which evaluated the use of tisagenlecleucel in the treatment of adult patients with relapsed or refractory FL after two or more lines of systemic therapy. A total of 98 patients were enrolled in the ELARA study, with 97 patients receiving an infusion of tisagenlecleucel. Of the 97 patients, 94 had measurable disease at baseline and were included in the efficacy analysis set (EAS). The primary endpoint was complete response rate (CRR) in the EAS. Secondary endpoints included overall response rate (ORR), duration of response (DoR), progression-free survival (PFS) and overall survival (OS). At the primary interim analysis (March 2021) with a median follow up of 16.59 months, the primary endpoint was met. In the EAS, CRR was 69.1% with a 95% CI 58.8 to 78.3, and the ORR was 86.2%. There was a subsequent data cut which showed that tisagenlecleucel continued to demonstrate highly durable

	efficacy, the latest report at median follow up of 29 months, CRR was 68.1%, the median PFS had not been reached, but the 24 month estimate for PFS was 57.4%. The median OS had not been reached, however the 24 month OS estimate was 87.7%, and median DoR had also not been reached, but the 24 month estimate was 66.4%. There is no evidence of a plateau in the curve and the responses appear durable. There is a desire among the clinicians to have tisagenlecleucel available for this patient cohort, and considers it an important treatment option for patients with poor prognostic features such as those who progress within 24 months of initial chemo-immunotherapy, and have progressed through two prior lines of therapy. It was noted that a relatively small number of patients would be eligible for treatment with tisagenlecleucel, representing less than 20% of the patient population. The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed. The relevant comparators were outlined, noting that there are limited treatment options for this patient cohort. The supporting evidence was discussed, noting at a recent report with a median follow up of 53 months, the study showed that the median OS had still not been reached and the median PFS was 53.3 months, representing a trend towards an improvement in PFS with tisagenlecleucel. The NCPE Review Group highlighted a number of limitations of the trial such the single arm and open label design, lack of mature survival data, and its non-comparative nature, for example, giving rise to the need to perform a comparative effectiveness analysis. The comparative effectiveness analysis was discussed and the results showed that there was a benefit for tisagenlecleucel across all relevant comparators, chemotherapy, idelalisib, and rituximab in combination with lenalidomide (R^2). In terms of safety, toxicities were in line with its known safety profile. The cost effectiveness analysis and the modelling used was outlined. In terms of the cost, tisagenlecleucel based on the price to the wholesaler at the time of the assessment (noting that the price was recently reduced), the total cost per patient is €350,919 including VAT and €281,228 excluding VAT. Comparatively the cost of chemotherapy is approximately [redacted]. The cost of chemotherapy in the double refractory population is [redacted]. The cost of idelalisib is [redacted]. It was noted that post HTA assessment the price to wholesaler for tisagenlecleucel was reduced and now costs €280,000. In terms of the results, in the Applicant's base case for the licensed population for tisagenlecleucel versus chemotherapy the ICER is €94,344/QALY. In the Applicant's base case for the double refractory population the ICER for tisagenlecleucel versus chemotherapy is €84,535/ QALY, for tisagenlecleucel versus idelalisib the ICER is €87,003/QALY, and for tisagenlecleucel versus R^2 the ICER is €73,225/QALY. In the NCPE-adjusted base case the ICER for tisagenlecleucel versus chemotherapy in the licensed population is €119,924/QALY, using the updated price to the wholesaler the ICER is €109,704/QALY. The NCPE-adjusted base case in the double refractory population the ICER for tisagenlecleucel versus chemotherapy is €126,172/QALY, for tisagenlecleucel versus idelalisib the ICER is €136,865/QALY, and for tisagenlecleucel versus R^2 the ICER is €123,706/QALY. Based on the analysis at the time of the assessment a reduction in the price to the wholesaler by 71.5% is required to meet the cost effectiveness threshold of €45,000 per QALY. In terms of the budget impact (BI), based on St James's hospital being the only designated CAR-T centre, at the time of the assessment it was indicated that the maximum number of patients that would be treated is 15 patients per year based on capacity constraints. This results in a net BI of €24.76 million including VAT over 5 years or €19.55 million excluding VAT. The NCPE recommends that tisagenlecleucel not be considered for reimbursement unless cost-effectiveness can be improved relative to existing treatments. The group noted the positive evidence and growing international experience in the use of tisagenlecleucel and other CAR- products. Having considered the clinical efficacy of the indication in this patient	

	cohort the committee members agreed by majority to recommend approval of this indication to the HSE Drugs Group subject to an improvement in cost. *(Decision: TRC 171)*	
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 Monday April 28th 2025	
6	**Any other business / Next meeting**	

The meeting concluded at 18.20pm.

Actions arising from meeting:

Ref.	Date of meeting	Details of action	Responsible	Update
25/03	31/03/2025	NCCP to communicate recommendations to HSE Drugs Group.	NCCP	Complete
25/03	31/03/2025	Apply for CPD	NCCP	Complete