National Cancer Control Programme

# NCCP Technology Review Committee (TRC)

## Meeting Notes

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| **Date of Meeting:** | **23rd September 2024 at 4.30pm** |
| **Venue:** | **Teleconference via MS Teams** |
| **Assessment:** | Pembrolizumab (Keytruda®) |
| | Teclistamab (Tecvayli®) |

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 | | |
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| NCPE representative | National Centre for Pharmacoeconomics (NCPE) | By MS Teams |
| Dr Oscar Breathnach | Medical Oncologist, Beaumont: ISMO nominee | By MS Teams |
| Dr Dearbhaile Collins | Consultant Medical Oncologist, Cork University Hospital: ISMO nominee **(Chair)** | By MS Teams |
| Dr Patrick Hayden | Consultant Haematologist, St James's :IHS representative | By MS Teams |
| Dr Susan Ahern | HTA Directorate: HIQA nominee | By MS Teams |
| **Non-member invited specialists present** | | |
| Dr Neil Barrett | Consultant Haematologist, Children's Health Ireland - Crumlin | |
| Dr Dearbhaile O'Donnell | Medical Oncologist, St. James's Hospital: ISMO nominee | |
| Prof Michael O'Dwyer | Consultant Haematologist, Galway :IHS representative | |
| Ms Fiona Mulligan | PCRS representative | |
| Dr Susan Spillane | HTA Directorate: HIQA nominee | |
| **Observers present** | | |
| Ms Elizabeth Breen | Chief II Pharmacist, NCCP | By MS Teams |
| Ms Helena Desmond | Senior Pharmacist, NCCP | By MS Teams |
| Prof Maccon Keane | Medical Oncologist, Galway | By MS Teams |
| Dr Derville O'Shea | Consultant Haematologist, Cork University Hospital | By MS Teams |

| Item | Discussion | Actions |
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| 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. | |
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| 2 | **Notes of previous meeting and matters arising** | |
| | The notes of the previous meeting on August 26th were reviewed and an amendment was made. | |
| 3 | **Drugs/Technologies for consideration** | |
| | **Pembrolizumab (Keytruda®) (Ref. TRC 158)**<br>*For the adjuvant treatment of patients with renal cell carcinoma (RCC) at increased risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions.*<br><br>The clinical aspects of this indication were discussed. The supporting evidence for this indication comes from the KEYNOTE-564 study, a phase III, international, randomised, double-blind, placebo-controlled clinical trial which evaluated the use of pembrolizumab as adjuvant therapy for the treatment of adult patients with RCC at increased risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions. At the latest data cut of September 2023, the study demonstrated a progression free survival (PFS) with an HR of 0.62, and an overall survival (OS) benefit at 48 months of 91% in the pembrolizumab group versus 86% in the placebo group, showing both a disease free and OS advantage. There is a strong desire among the clinicians to have pembrolizumab available for the adjuvant treatment of RCC, currently there are no other treatment options available for this small patient cohort. It was noted that pembrolizumab is a drug that clinicians know well, due to its use in other cancers such as melanoma and lung for example.<br><br>The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed. The supporting evidence was outlined, noting that the data from the June 2021 data cut was used to inform the NCPE assessment, as the most recent data cut of September 2023 was not available at the time of the NCPE assessment. Based on that the June 2021 data cut, the data was considered immature, the disease-free survival (DFS) HR was 0.63, only 4.6% of patients had died and the HR for OS was 0.52. The NCPE Review Group highlight a number of limitations regarding the supporting evidence, the key limitation being the immaturity of the data. The cost effectiveness analysis was discussed and the modelling used was outlined. The cost effectiveness of adjuvant pembrolizumab is dependent on long term disease free survival translating into an OS benefit, giving rise to uncertainty. In terms of cost, the cost per treatment course of pembrolizumab for a duration of 1 year based on 17 cycles is [redacted]. The cost of routine surveillance, the current standard of care (SOC) for this patient cohort is not associated with any drug cost. The Applicant's base case ICER was €37,705 per QALY. A number of changes were made to the NCPE-adjusted base case and the NCPE adjusted base case is €86,073 per QALY. A 40.6% reduction in the price to wholesaler would be required to meet the willingness to pay threshold. In terms of the budget impact (BI) it is estimated that 49 patients will be treated in year 1, rising to 70 patients by year 5. The cumulative 5-year gross BI was estimated to be €31.45 million including VAT, or €25.13 million excluding VAT, noting that the gross BI is equal to the net BI, as the current SOC of routine surveillance is not associated with any drug cost. The NCPE recommends that pembrolizumab be considered for reimbursement, for this indication, if cost-effectiveness can be improved relative to existing treatments.<br><br>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. | |

*(Decision: TRC 158)*

Teclistamab (Tecvayli®) (**Ref. TRC 159)**

*As monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.*

The clinical aspects of this indication were discussed. It was noted that teclistamab is available via a compassionate use programme (CUP) at St James's Hospital (SJH), where 10 patients were treated over 12 months. The supporting evidence for this indication is the MajesTEC-1 trial, a single arm, open-label, multicentre trial which investigated the use of teclistamab for the treatment of adult patients with refractory (RR) multiple myeloma (MM), who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody and have demonstrated disease progression on the last therapy. Treatment with teclistamab proposes a risk of cytokine release syndrome (CRS), with a clinically significant risk in ≤2% of patients and up to 60% of patients experience fever in the first few days of treatment. Teclistamab is initially administered in step-up doses to reduce the risk of CRS, in which patients require an inpatient stay for up to 8 days. It was noted that in the United States, administration is slowly being migrated to the outpatient setting, whereas across Europe, administration is in the inpatient setting. Following the step-up dosing, a maintenance dose is administered once weekly, and for those who achieve a compete response (CR) for a minimum of 6 months, then a dosing frequency of every two weeks may be considered. It was noted that for those who achieve a CR, dosing frequency could be further reduced to once a month, however this is not licensed. In the MajesTEC-1 trial, after 14 months of follow up the overall response rate (ORR) was 63%, and the median duration of response (DOR) was 18.4 months. Over all the median progression free survival (PFS) was 11.4 months, similar to that of the 10 patients treated at SJH via the CUP. The safety profile of teclistamab was discussed, 94% of patients experienced at least one adverse event of ≥ Grade 3. Frequent adverse reactions of any grade in patients were hypogammaglobinaemia, CRS, and mild neutropenia and anaemia. There was a high incidence of infection, however it was noted that the incidence of infection in clinical practice is nothing like the levels seen the MajesTEC-1 trial, and it is considered that teclistamab is well tolerated patients are on regular prophylaxis and receive immunoglobins. In the MajesTEC-1 Trial, there were a higher rate of infection experienced compared to that currently seen in clinical practice, however it was noted that the trial was conducted during Covid19, which would explain the discrepancy in terms of infections. Teclistamab's place in therapy was discussed, as a fourth line alternative treatment option for RRMM, and there is desire among the clinicians to have this highly effective treatment available for this patient cohort.

The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed. The positioning of teclistamab in the current treatment pathway was discussed and the relevant comparators were outlined, noting that this is a rapidly evolving area, and a number of new treatments have been licensed, but not yet reimbursed. The supporting evidence was outlined, in terms of the data, the ORR was 63% at the final analysis (August 2023), OS data was 57% mature at that date and was considered immature. The median OS was 22.2 months and the PFS data was 65% mature with a median PFS of 11.4 months. The NCPE Review Group highlighted a number of limitations regarding the supporting evidence, such as the single arm, open label nature of the study, small sample size and lack of direct comparator evidence, the generalisability of the trial population, the median age of the trial participants was 63.9 years with an ECOG of 0-1, while clinical opinion indicated that in Irish clinical practice this patient

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| | population is most likely to be around 70 years and less fit. The immaturity of the OS data was also considered a limitation, while the ORR was good, there is uncertainty whether this will translate into an improvement in OS. In terms of an indirect treatment comparison (ITC), data from the LocoMMotion and MoMMent studies (representing real world evidence) and the CARTITUDE 1 trial. The cost effectiveness analysis was discussed and the modelling used was outlined. In terms of cost, the cost per treatment course of teclistamab is €196,983 including VAT and €157,415 excluding VAT, based on median treatment duration, possibility underestimating the mean treatment cost, but mirrors the licensed doing of every two weeks after six months. The Applicant's base case ICER was €128,269 per QALY. A number of changes were made to the NCPE-adjusted base case and the NCPE adjusted base case is €188,452 per QALY. There is 0% probabilities of cost effectiveness at both thresholds (€20,000/QALY and €45,000/QALY) in both the Applicant and the NCPE- adjusted base case. To meet the €45,000/QALY threshold, a 69.89% reduction in the price to wholesaler is required. It was noted that a PAS offer was not submitted by the Applicant. In terms of the budget impact (BI), it is estimated that 36 patients will be treated in year 1 and 21 in year 5. The 5-year gross BI is estimated to be €30 million including VAT and €24 million excluding VAT. The estimated 5-year net BI is €23.2 million including VAT and €18.2 million excluding VAT. The NCPE recommends that teclistamab not be considered for reimbursement unless cost-effectiveness can be improved relative to existing treatments.<br><br>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.<br><br>*(Decision: TRC 159)* | |
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| **4** | **Update on other drugs in the reimbursement process** | |
| | An update had been shared with the group in the documentation for the meeting | |
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| **5** | **Next meeting** | |
| | The proposed date for the next meeting is October 21st 2024 | |
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| **6** | **Any other business / Next meeting** | |
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The meeting concluded at 17.35pm.

**Actions arising from meeting:**

| Ref. | Date of meeting | Details of action | Responsible | Update |
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| 24/01 | 23/09/2024 | NCCP to communicate recommendations to HSE Drugs Group. | NCCP | Complete |
| 24/01 | 23/09/2024 | Apply for CPD | NCCP | Complete |
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