HSE Drugs Group – April 2023 Minutes

Meeting 2023.04: Tuesday 18th April 2023, 14.00 – 16.30

Via videoconference

1. Draft Minutes for Consideration

The minutes of the March 2023 meeting were considered and approved.

2. Matters arising / Update on Medicines considered at previous meeting

i. An update on items previously considered by the Drugs Group was provided. All relevant Drugs Group recommendations, including March 2023 Drugs Group recommendations, had been approved by the HSE Executive Management Team (EMT). The Group noted the referral of Risdiplam to the HSE Medicines Management Programme for the progression of a managed access protocol to support reimbursement under the High Tech arrangements. The Group was also provided with an update on the estimated net financial impact to the HSE over 5 years of the 2023 EMT positive approvals thus far.

ii. [redacted]

3. Declaration of Interests / Nil Interest

None declared

4. Medicines for Consideration

i. 21012 Inhaled liposomal amikacin (Arikayce®) for the treatment of non-tuberculosis mycobacterial (NTM) lung infections

The Drugs Group considered Inhaled Amikacin Sulfate (ARIKAYCE Liposomal®) for the treatment of non-tuberculous mycobacterial (NTM) lung infections caused by *Mycobacterium avium* Complex (MAC) in adults with limited treatment options who do not have cystic fibrosis. Inhaled Amikacin Sulfate had previously been considered by the Drugs Group at the June 2021 meeting. At this meeting the Group concluded that ARIKAYCE Liposomal® was a high cost treatment which required a full Health Technology Assessment and that a robust deliberation could not take place in its absence. The applicant company responded to this ask by submitting a dossier for assessment.

The Group reviewed again the clinical evidence from study INS-212, a randomised, open-label trial in adult patients with non-tuberculous mycobacterial lung infections caused by MAC. In Study INS-212 (CONVERT), patients who had not achieved sputum culture conversion (SCC) while being treated with Multiple Drug Regimen(s) (MDR) for at least 6 months before study entry were randomised to receive ARIKAYCE Liposomal® in addition to their MDR treatment or to continue with MDR alone. A total of 335 patients were randomised and dosed (ARIKAYCE liposomal + MDR n = 223; MDR alone n = 112). Sixty-five (29.0%) and 10 (8.9%) patients achieved SCC by month 6 on treatment in the ARIKAYCE liposomal + MDR and the MDR group, respectively ($p < 0.0001$). Of these, based on

the primary analysis durable SCC at 3 months off treatment was achieved by 16.1% [36/224] vs. 0% [0/112]; p<0.0001.

The Group recognised that ARIKAYCE Liposomal® is the first approved treatment in the EU specifically for NTM lung infections in adults caused by MAC and with limited treatment options. The Drugs Group by majority recommended reimbursement under the High Tech arrangements. In making its positive reimbursement recommendation, the Group noted the unmet need, a relatively modest overall drug budget impact, the totality of the clinical evidence available and clinical opinion provided through Antimicrobial Resistance & Infection Control (AMRIC) in 2020, which supported inhaled Amikacin Sulfate reimbursement (in line with the licensed indication) on the basis of a recommendation from a Consultant Microbiologist, Infectious Disease Physician or Consultant Respiratory Physician. The majority position was conditional on oversight of use being provided through AMRIC guidelines and monitoring.

ii. 23005 Nivolumab (Opdivo®) + Ipilimumab (Yervoy®) for metastatic colorectal cancer

The Drugs Group considered Nivolumab (Opdivo®) in combination with Ipilimumab (Yervoy®) for the treatment of adult patients with mismatch repair deficient or microsatellite instability-high metastatic colorectal cancer after prior fluoropyrimidine-based combination chemotherapy. The Group reviewed the clinical and economic evidence in detail as well as the advice emanating from the National Cancer Control Programme Technology Review Committee (NCCP TRC).

The Group reviewed the clinical evidence for the regulatory approval of this indication which came from CheckMate-142, a Phase 2, multi-centre, open-label, single-arm study (n=119). The primary outcome measure was investigator-assessed overall response rate (ORR). Secondary outcome measures were blinded independent central review (BICR)-assessed ORR and disease control rate. Analysis of ORR included duration of and time to response. Exploratory outcome measures included progression free survival (PFS) and overall survival (OS). The investigator-assessed objective response rate was 64.7% (77/119; 95% CI 55.4 to 73.2) at the October 2020 interim analysis (median duration of follow up was 51.1months). BICR assessments were generally consistent with the investigator assessment. Confirmed responses were observed regardless of BRAF or KRAS mutation status and tumour PD-L1 expression levels. Median OS and median investigator-assessed PFS were not reached.

The Group noted that the proposed commercial offering resulted in ICERs ranging from [redacted] (applicant base case, Nivo + Ipi vs FOLFIRI + Bevacizumab) to [redacted] (NCPE adjusted base case, Nivo+Ipi vs BSC). The Drugs Group unanimously recommended reimbursement of Nivolumab + Ipilimumab for this indication under the ODMS on the basis of the evidence submitted.

iii. 23006 Cefiderocol (Fetcroja®) for infections due to aerobic Gram-negative organisms in adults with limited treatment options

The Drugs Group considered Cefiderocol (Fetcroja®) for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options. The Drugs Group acknowledged the clinical burden of multi-drug resistant pathogens and that there is a high unmet medical need for additional antibacterial agents addressing resistance in Gram-negative organisms.

The Group reviewed the clinical and economic evidence in detail and acknowledged that the pivotal data for the assessment of efficacy and the adequacy of the dose of Cefiderocol for the intended indication are the in-vitro data and the most directly relevant dataset for the indication and target population applied for is that from the CREDIBLE-CR study.

The Drugs Group acknowledged that Cefiderocol is a high cost antimicrobial agent and represents a price premium over the current standard of care. On the basis of the unmet need arising through antimicrobial resistance, the limited use expected in clinical practice and oversight provided through Antimicrobial Resistance & Infection Control (AMRIC) the Drugs Group unanimously recommended reimbursement if a [redacted], was forthcoming.

iv. 23007 Pembrolizumab (Keytruda®) in combination with chemotherapy for locally advanced unresectable or metastatic carcinoma of the oesophagus or HER-2 negative gastroesophageal junction adenocarcinoma

The Drugs Group considered Pembrolizumab (Keytruda®) in combination with platinum and fluoropyrimidine-based chemotherapy for the first-line treatment of locally advanced unresectable or metastatic carcinoma of the oesophagus or HER-2 negative gastroesophageal junction adenocarcinoma, in adults whose tumours express PD-L1 with a CPS ≥ 10. The Group reviewed the clinical and economic evidence in detail as well as the advice emanating from the National Cancer Control Programme Technology Review Committee (NCCP TRC).

The Group reviewed the clinical evidence from the pivotal KEYNOTE-590 study supporting marketing authorisation of this indication which was a phase III, double-blind, randomised controlled trial designed to evaluate the safety and efficacy of Pembrolizumab in combination with cisplatin and 5-FU (herein Pembrolizumab plus chemotherapy) versus cisplatin and 5-FU. The trial recruited an 'all-comer' population (i.e. did not restrict recruitment by PD-L1 status). A total of 749 participants were randomised. Of those, 383 participants had tumours which expressed PD-L1 CPS ≥10 (Pembrolizumab plus chemotherapy n=186; chemotherapy n=197). The co-primary endpoints were progression-free survival (PFS) and overall survival (OS) in the overall population and subpopulation of patients whose tumours were positive for PD-L1 with CPS ≥10, with comparisons adjusted to control for multiplicity. At the July 2021 data cut-off, median PFS in the CPS ≥10 subpopulation was 7.5 months with Pembrolizumab plus chemotherapy versus 5.5 months with chemotherapy (HR 0.51; 95% confidence interval [CI] 0.41, 0.65). At the same data cut-off, median OS was 13.6 months with Pembrolizumab plus chemotherapy versus 9.4 months with chemotherapy (HR 0.64; 95% CI 0.51, 0.80).

The group noted that to improve cost-effectiveness vs SoC chemotherapy the applicant company (MSD) proposed to apply a [redacted] The proposed commercial offering resulted in ICERs that were [redacted]. The Drugs Group by majority recommended reimbursement on the basis of the unmet need and clinical and cost effectiveness evidence presented.

v. 23008 Nivolumab (Opdivo®) in combination with chemotherapy for unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma (OSCC)

The Drugs Group considered Nivolumab (Opdivo®) in combination with fluoropyrimidine- and platinum-based combination chemotherapy for the first-line treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma with tumour cell PD-L1 expression ≥ 1%. The Group reviewed the clinical and economic evidence in detail as well as the advice emanating from the National Cancer Control Programme Technology Review Committee (NCCP TRC).

The Drugs Group unanimously recommended reimbursement of this indication on the basis of the clinical efficacy. In light of Pembrolizumab (Keytruda®) in combination with chemotherapy for locally advanced unresectable or metastatic carcinoma of the oesophagus or HER-2 negative gastroesophageal junction adenocarcinoma previously being recommended for reimbursement, which is considered to be the main comparator, [redacted]

Appendix 1: Members Present on Microsoft Teams

Member	Title	Attendance
Prof. Áine Carroll	Chair, Medical Consultant	In attendance
Mr Shaun Flanagan	Primary Care Reimbursement Service (Assistant National Director)	In attendance
Ms Aoife Kirwan	Public Interest Member	Apologies received
Dr David Hanlon	National Clinical Advisor and Group Lead Primary Care (General Practitioner)	In attendance
Ms Patricia Heckmann for Professor Risteárd Ó Laoide	Chief Pharmacist, National Cancer Control Programme for National Director of the National Cancer Control Programme (Medical Consultant)	In attendance
Dr Philip Crowley	National Director for Quality Improvement (Medical Doctor)	In attendance
Dr Valerie Walshe	Office of the Chief Financial Officer (Economist, PhD)	In attendance*
Post Vacant	Office of Nursing & Midwifery Services (Director of Nursing)	n/a
Dr Roy Browne	Mental Health Division (Consultant Psychiatrist)	Apologies received
Dr Cliona McGovern	Public Interest Member / Ethicist	In attendance
Mr Michael Power	Public Interest Member	In attendance
Dr Anne Dee	Specialist in Public Health Medicine	In attendance
Post Vacant	Acute Operations Division (Assistant National Director)	n/a
Prof Ellen Crushell	Consultant in Inherited Metabolic Disorders	In attendance*
Dr Lisa Cogan	Consultant in Medicine for the Elderly, Medical Director, Royal Hospital Donnybrook	In attendance*

*parts of meeting and voting not attended

In attendance (non-voting):
Professor Michael Barry (NCPE)

Secretariat:
Ellen McGrath, Chief I Pharmacist, Head of CPU PCRS
Jennifer McCartan, Chief II Pharmacist, CPU PCRS
Mary Staunton, Chief II Pharmacist, CPU PCRS
Louise Walsh, Senior Pharmacist, CPU PCRS