HSE Drugs Group – November 2021 Minutes

Meeting 2021.09: Tuesday 9th November 2021, 14.00 – 16.00

Via videoconference

1. Draft Minutes for Consideration

The minutes of the October 2021 meeting were considered and approved.

2. Confidentiality forms

It had previously been agreed that all members (including public servants) would sign confidentiality forms (once off action).

3. Matters arising / Update on Medicines considered at previous meetings

An update on items previously considered by the Drugs Group was provided. A number of new medicines / new indications approvals are anticipated to progress in December 2021.

4. Declaration of Interests / Nil Interest

5. Medicines for Consideration

i. 21026 Esketamine for treatment-resistant major depressive disorder

The Drugs Group considered Esketamine (Spravato®) in combination with a SSRI or SNRI, for adults with treatment-resistant major depressive disorder, who have not responded to at least 2 different treatments with antidepressants in the current moderate to severe depressive episode. The Drugs Group noted that despite the availability of many antidepressant pharmacotherapies, Esketamine (Spravato®) represented the first licensed medicinal product for treatment-resistant depression in Europe. It was acknowledged that many oral antidepressants require several weeks before a full clinical effect on depressive symptoms is evident. The Group recognised there was an unmet need for efficacious, licensed pharmacotherapies with a more rapid onset of action for the treatment of this debilitating disorder.

The Drugs Group reviewed the clinical evidence for Esketamine (Spravato®) which included both short-term and longer-term trials. The complexities of conducting clinical trials in this population were noted. In TRANSFORM-2, Esketamine plus a newly initiated oral antidepressant demonstrated a statistically significant and clinically meaningful change in the MADRS total score from baseline to day 28 compared to a newly initiated oral antidepressant plus placebo. Clinically meaningful treatment effects in change in MADRS total scores were also observed to favour the Esketamine + oral antidepressant arms compared to the control arms in TRANSFORM-1 and TRANSFORM-3 but were not statistically significant. The Group noted symptom reduction was observed as early as 24 hours post-dose. Results from the SUSTAIN-1 study demonstrated that the treatment effect of Esketamine + oral antidepressant was maintained in the longer term. Esketamine is classified as a controlled drug under the Misuse of Drugs Regulations 2017, Schedule 3 (2). The Group acknowledged that the considerable administration and post-dose observation requirements for Esketamine (Spravato®) were sufficient to alleviate concerns regarding misuse of this drug.

The Group noted that the considerable uncertainties in the economic model partly arose from the limitations of the clinical evidence. Following extensive and protracted deliberations on the totality of clinical and cost-effectiveness evidence, the Drugs Group agreed that the confidential price proposed by the applicant was of insufficient magnitude for the Group to support reimbursement. The Drugs

Group unanimously agreed that it would recommend reimbursement if [redacted]

ii. 21027 Pembrolizumab + Axitinib for renal cell carcinoma

The Drugs Group considered Pembrolizumab (Keytruda®) in combination with Axitinib for the first-line treatment of advanced renal cell carcinoma (RCC) in adults. This was the first application for a combination regimen of an immune checkpoint inhibitor and a VEGF-targeting tyrosine kinase inhibitor in RCC to be reviewed by the Group. The Group noted that the current treatment landscape for advanced RCC is dynamic and evolving. An alternative immune checkpoint inhibitor treatment regimen was reimbursed by the HSE in early 2021 for patients with intermediate / poor-risk advanced RCC.

The clinical evidence from the pivotal KEYNOTE-426 study was reviewed by the Drugs Group. The results from interim analyses demonstrated that progression-free survival (PFS) and overall survival (OS) were significantly longer with Pembrolizumab plus Axitinib compared with Sunitinib. Median overall survival has not yet been reached and results are immature. The lack of monotherapy experimental arms in the pivotal study hampered the assessment of the contribution of each component of the combination treatment. In PFS and OS subgroup analyses, the Group noted a lower treatment effect for the favourable IMDC risk group was observed compared to the intermediate and poor-risk IMDC risk groups.

Pembrolizumab and Axitinib are expensive medicines with incremental cost-effectiveness ratios (ICERs) exceeding conventional willingness to pay thresholds, most notably in the intermediate / poor-risk group versus the comparator Nivolumab + Ipilimumab. The Group reviewed the impact of the commercial offer for Pembrolizumab on the cost-effectiveness estimates and budget impact. Following consideration of the clinical need, the clinical evidence, the considerable cost-effectiveness estimates, and the substantial budget impact of this regimen (notwithstanding the commercial offer), the Drugs Group unanimously agreed that it could not support reimbursement of this combination regimen for advanced RCC.

iii. 21029 Trastuzumab emtansine for adjuvant treatment of HER2-positive early breast cancer

The Drugs Group considered Trastuzumab emtansine (Kadcyla®) for the adjuvant treatment of adult patients with HER2-positive early breast cancer who have residual invasive disease, in the breast and/or lymph nodes, after neoadjuvant taxane-based and HER2-targeted therapy. The Group noted the pivotal KATHERINE study met its primary endpoint. A clinically meaningful and statistically significant improvement in Invasive Disease-Free Survival (IDFS) was observed in patients who received Trastuzumab emtansine compared with Trastuzumab. Overall Survival (OS) data remain immature, although an OS benefit trend was observed favouring Trastuzumab emtansine over Trastuzumab. The Group noted that Trastuzumab emtansine was cost-effective at the conventional €45,000 / QALY willingness to pay threshold at list price. The impact of the commercial offer further improved the cost-effectiveness of Trastuzumab emtansine versus Trastuzumab. The Drugs Group unanimously recommended in favour of reimbursement of Trastuzumab emtansine in this indication.

iv. 21030 Neratinib as extended adjuvant treatment of early-stage breast cancer

There was insufficient time for the Drugs Group to conclude deliberations on this application. This will be carried forward to the December 2021 meeting.

v. 20131 Pembrolizumab for relapsed or refractory classical Hodgkin Lymphoma

There was insufficient time for the Drugs Group to conclude deliberations on this application. This will be carried forward to the December 2021 meeting.

6. AOB

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	In attendance
Dr David Hanlon	National Clinical Advisor and Group Lead Primary Care (General Practitioner)	In attendance
Professor Risteárd Ó Laoide	National Director of the National Cancer Control Programme (Medical Consultant)	Apologies received
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
Ms Joan Donegan	Office of Nursing & Midwifery Services (Director of Nursing)	Apologies received
Dr Roy Browne	Mental Health Division (Consultant Psychiatrist)	In attendance
Dr Cliona McGovern	Public Interest Member / Ethicist	In attendance
Mr Michael Power	In attendance	In attendance
Post Vacant	Health and Wellbeing Division (Public Health Physician)	n/a
Ms Angela Fitzgerald	Acute Services Division (Assistant National Director)	In attendance*
Prof Ellen Crushell	Consultant in Inherited Metabolic Disorders	Apologies received
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):
Ms Kate Mulvenna
Professor Michael Barry (NCPE)

Secretariat:
Ms Jennifer McCartan, Chief II Pharmacist, CPU PCRS
Ms Fiona Mulligan, Chief II Pharmacist, CPU PCRS