HSE Drugs Group – November 2023 Minutes

Meeting 2023.10: Tuesday 14th November 2023, 14.00 – 16.30

Via videoconference

1. Draft Minutes for Consideration

The minutes of the October 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 from previous meetings had been progressed to the HSE Executive Management Team (EMT). The number of items that had been considered in the first nine meetings of the Drugs Group in 2023 was shared with the group. The Drugs Group were also notified that in 2023 (as of the date of the meeting) 31 new medicines and new uses of existing medicines have been approved for reimbursement/hospital pricing approval by the HSE.

3. Declaration of Interests / Nil Interest

None declared

4. Medicines for Consideration

i. **23006 Cefiderocol (Fetcroja®) for infections due to aerobic Gram-negative organisms in adults with limited treatment options. (NCPE HTA ID: 22003)**

The Drugs Group considered Cefiderocol (Fetcroja®) for the treatment of infections due to aerobic Gram-negative organisms in adults with limited treatment options. Cefiderocol had previously been considered by the Drugs Group at the April 2023 meeting. At this meeting the Group acknowledged that whilst Cefiderocol is a high cost antimicrobial agent and represents a price premium over the current standard of care, there is a high unmet medical need for additional antibacterial agents addressing resistance in Gram-negative organisms. The Drugs Group were in favour of progressing a positive recommendation without a requirement for a HTA at the April 2023 meeting if a [redacted] was forthcoming.

The applicant company responded to this requirement by submitting a revised commercial offering for consideration. The applicant proposed a confidential [redacted]

Given the high unmet need, the Drugs Group unanimously recommended hospital pricing approval of Cefiderocol, subject to the revised commercial offering and appropriate antimicrobial stewardship.

ii. **23026 Inclisiran (Leqvio®) for adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia (NCPE HTA ID: 20051)**

The Drugs Group considered Inclisiran (Leqvio®) for the treatment of adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet. A subgroup of the product licence was proposed by the applicant as per the three subpopulations considered in the economic model: (i) Adults with a history of ASCVD (ASCVD population); (ii) adults with a history of HeFH who have not previously experienced a CV event (HeFH

primary prevention population); (iii) adults who have not previously experienced a CV event but are at higher risk of doing so compared to the general population (Primary Prevention of patients at elevated risk [PPER] population). All patients in all subpopulations were assumed to have baseline LDL-C levels ≥2.6mmol/L despite treatment with a maximum tolerated dose (MTD) of statin therapy +/- ezetimibe.

The Drugs Group reviewed the entirety of the available clinical and economic evidence as well as the outputs of commercial negotiations. The Group noted that the effect of Inclisiran on cardiovascular morbidity and mortality has not yet been determined and that the Inclisiran cardiovascular outcomes trial, ORION-4, is ongoing and will determine whether Inclisiran reduces the incidence of adverse cardiovascular events in patients with pre-existing atherosclerotic cardiovascular disease. The primary outcome is the number of participants with a major adverse cardiovascular event (MACE) defined as time to first occurrence of coronary heart disease (CHD) death; myocardial infarction; fatal or non-fatal ischemic stroke; or urgent coronary revascularisation procedure. The estimated primary completion date is July 2026.

On the basis of the entirety of the evidence presented, the outstanding clinical uncertainty coupled with the significant budget impact and unidentified unmet need, the Drugs Group unanimously recommended against hospital pricing approval of Inclisiran (Leqvio®).

iii. 23027 Maribavir (Livtencity®) for the treatment of cytomegalovirus (CMV) infection (NCPE HTA ID: 22069)

The Drugs Group considered Maribavir (Livtencity®) for the treatment of cytomegalovirus (CMV) infection and/or disease that is refractory (with or without resistance) to one or more prior therapies, including ganciclovir, valganciclovir, cidofovir or foscarnet in adult patients who have undergone a haematopoietic stem cell transplant (HSCT) or solid organ transplant (SOT).

The Drugs Group reviewed the entirety of the available clinical and economic evidence as well as the outputs of commercial negotiations.

The Group reviewed the evidence from the pivotal phase III, multi-centre, randomised, open-label, active-controlled study (SOLSTICE) which assessed the efficacy and safety of Maribavir treatment compared to investigator-assigned treatment (IAT) in transplant recipients with CMV infections that are refractory or resistant to treatment with ganciclovir, valganciclovir, foscarnet, or cidofovir including CMV infections with or without confirmed resistance to one or more anti-CMV agents. Patients were stratified by transplant type (HSCT or SOT) and screening CMV DNA levels and then randomised in a 2:1 ratio to receive Maribavir 400 mg twice daily (n=235) or IAT (n=117) (ganciclovir, valganciclovir, foscarnet, or cidofovir) for an 8-week treatment period and a 12 week follow-up phase. The primary efficacy endpoint was confirmed CMV viraemia clearance (plasma CMV DNA concentration below the lower limit of quantification (< LLOQ; i.e., < 137 IU/mL) at Week 8 regardless of whether either study-assigned treatment was discontinued before the end of the stipulated 8 weeks of therapy. For the primary endpoint, Maribavir was superior to IAT (55.7% vs. 23.9%, respectively, $p < 0.001$), Maribavir, n=131/235; IAT, n=28/117 (difference 95% CI: 32.8%; 22.8-42.7; $p<0.001$).

The Drugs Group unanimously recommended reimbursement of Maribavir on the basis of the unmet need, the clinical evidence that was considered in conjunction with a commercial offer submitted by the applicant that substantially reduced the anticipated budget impact to treat a limited number of patients expected to be eligible for treatment in this setting.

iv. 23028 Osimertinib (Tagrisso®) for the adjuvant treatment of NSCLC (NCPE HTA ID: 21066)

The Drugs Group considered Osimertinib (Tagrisso®) for the adjuvant treatment after complete tumour resection in adult patients with stage IB-IIIA non-small cell lung cancer (NSCLC) whose tumours have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations.

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) and the outputs of commercial negotiations. The Group acknowledged that despite progress in early detection and treatment, NSCLC is most often diagnosed at an advanced stage and has a poor prognosis.

The Group reviewed the clinical efficacy data from ADAURA, a phase III, double-blind, randomised, placebo-controlled trial which assessed the safety and efficacy of Osimertinib versus placebo, in patients with stage IB-IIIA EGFR-mutated (ex19del or L858R) NSCLC who have undergone complete tumour resection, with or without post-operative adjuvant chemotherapy. Eligible patients were randomised 1:1 to Osimertinib (n=339) or placebo (n=343). The primary endpoint was investigator-assessed disease-free survival (DFS). Overall survival (OS) was a key secondary endpoint. The April 2022 data cut-off indicated that Osimertinib had a median DFS of 65.8 months (95% CI 61.7 to non-calculable) compared with 28.1 months (95% CI 22.1 to 35.0) for placebo (HR 0.27; 95% CI 0.21 to 0.34). The final analysis of OS (data cut-off: 27 January 2023) demonstrated a statistically significant improvement in OS for patients treated with Osimertinib compared to placebo. The five-year OS rate was 88% (95% CI 83 to 91) in the Osimertinib arm and 78% (95% CI 73 to 82) in the active monitoring arm. The HR for OS was 0.49 (95.03% CI, 0.34 to 0.70) p<0.001. For both populations, the median OS was not reached in either treatment arm and the 95% CIs were not calculable.

At list price the ICER for Osimertinib in this indication ranged from €57,892/QALY (applicant base case) to €70,595/QALY (under NCPE preferred assumptions) versus Active monitoring. The applicant (AstraZeneca) offered a [redacted]. Under the NCPE preferred assumptions, the ICER resultantly decreased to [redacted]/QALY. The Drugs Group recognised the substantial improvement in cost-effectiveness and by majority voted in favour of reimbursement.

v. 23029 Tezepelumab (Tezspire®) for severe asthma (NCPE HTA ID: 23025)

There was insufficient time for the Drugs Group to conclude deliberations on this application. This will be carried forward to the December 2023 meeting.

5. AOB

The 2024 Drugs Group proposed meeting dates were shared with the Group.

Appendix 1: Members Present on Microsoft Teams

Member	Title	Attendance
Prof. Áine Carroll	Chair, Medical Consultant	Apologies received
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)	Apologies received
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 (Acting chair)
Dr Valerie Walshe	Office of the Chief Financial Officer (Economist, PhD)	In attendance
Clare Mac Gabhann	Director of Nursing and Midwifery (Prescribing)	In attendance
Position vacant	Mental Health Division (Consultant Psychiatrist)	N/A
Dr Cliona McGovern	Public Interest Member / Ethicist	Apologies received
Mr Michael Power	Public Interest Member	Apologies received
Dr Anne Dee	Specialist in Public Health Medicine	In attendance
Catherine Clarke	Strategy & Planning – Unscheduled Care (Assistant National Director)	In attendance
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

In attendance (non-voting):
Dr Laura McCullagh (NCPE)

Secretariat:
Ellen McGrath, Head of CPU PCRS
Fiona Mulligan, Chief II Pharmacist, CPU PCRS
Mary Staunton, Chief II Pharmacist, CPU PCRS
Louise Walsh, Senior Pharmacist, CPU PCRS