HSE Drugs Group – September 2023 Minutes

Meeting 2023.08: Tuesday 12th September 2023, 14.00 – 16.30

Via videoconference

1. Draft Minutes for Consideration

The minutes of the August 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. Two negative recommendations from the May 2023 meeting have yet to be progressed to the HSE EMT as specific information sought by the Group, to be presented alongside the recommendation(s), remains outstanding. This is being followed up by the HSE CPU.

ii. The projected significant new drug funding anticipated to be required in 2024 was also brought to the attention of the Drugs Group for awareness.

3. Declaration of Interests / Nil Interest

None declared

4. Medicines for Consideration

i. 22011 Bempedoic Acid and Bempedoic Acid in combination with Ezetimibe (NCPE HTA ID: 20026a & 20026b)

The Drugs Group considered Bempedoic Acid (Nilemdo®) and Bempedoic Acid plus Ezetimibe (Nustendi®) for the treatment of adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet. Bempedoic Acid (Nilemdo®) and Bempedoic Acid plus Ezetimibe (Nustendi®) were previously considered by the Drugs Group at the April 2022 meeting. At this meeting the Drugs Group noted that at that point in time the effect of Bempedoic Acid on cardiovascular outcomes had not yet been determined. The Drugs Group concluded that the results from the then ongoing CLEAR Outcomes trial were required to inform deliberations.

Results of the event-driven CLEAR Outcomes trial were published in 2023.

The Group reviewed the clinical and economic evidence in detail and the outputs of further commercial negotiations conducted in August 2023. CLEAR Outcomes was a double-blind, randomised, placebo-controlled trial involving high risk cardiovascular disease (CVD) patients who were unable or unwilling to take statins. The primary outcome was a four-component composite of major adverse CV events (MACE) defined as death from CV causes, nonfatal myocardial infarction (MI), nonfatal stroke, or coronary revascularisation (MACE-4). The study showed that treatment with Bempedoic Acid reduced the risk of a MACE-4 in patients with high and very high CV risk with elevated LDL-cholesterol and who are intolerant to statins. A MACE-4 event occurred in 11.7% (n=819) Bempedoic Acid-treated patients and 13.3% (n=927) placebo-treated patients. Bempedoic Acid reduced the risk of experiencing a MACE-4 event by 13% versus placebo (hazard ratio [HR]: 0.87, 95%CI: 0.79, 0.96); p=0.004).

The Drugs Group unanimously recommended reimbursement of Bempedoic Acid (Nilemdo®) and Bempedoic Acid plus Ezetimibe (Nustendi®), subject to a managed access protocol being put in place on the basis of the evidence presented.

ii. 23020 Azacitidine (Onureg®) for maintenance treatment in acute myeloid leukaemia (AML) (NCPE HTA ID: 22070)

The Drugs Group considered Azacitidine (Onureg®) for use as maintenance therapy in adult patients with acute myeloid leukaemia (AML) who achieved complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following induction therapy with or without consolidation treatment and who are not candidates for, including those who choose not to proceed to, hematopoietic stem cell transplantation (HSCT).

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 AML is a rare and aggressive malignancy characterized by rapid progression and is uniformly fatal if not treated and that effective maintenance therapy could provide an important therapeutic approach for a disease associated with short survival and a high unmet medical need.

The Group reviewed the clinical efficacy data from QUAZAR AML-001, a phase III, randomised, double-blind, placebo-controlled, multi-centre study which evaluated Azacitidine (Onureg®) versus placebo as maintenance therapy in AML patients. A total of 472 patients were randomised 1:1 between Azacitidine (Onureg®) and placebo treatment arms. The primary endpoint was Overall Survival (OS). The median OS was 24.7 months for the oral azacitidine group vs 14.8 months for the placebo group after a median follow-up time of 41.2 months. The hazard ratio (HR) was 0.69 (95% confidence interval [CI]: 0.55, 0.86), indicating a 31% reduction in the risk of death for the oral azacitidine group.

The Drugs Group unanimously recommended reimbursement of oral Azacitidine on the basis of the unmet need, the clinical evidence and the substantial commercial offer submitted by the applicant [redacted]

iii. 23021 Fostemsavir (Rukobia®) for HIV (NCPE HTA ID: 23018)

The Drugs Group considered Fostemsavir (Rukobia®) in combination with other antiretrovirals, indicated for the treatment of adults with multidrug resistant (MDR) HIV-1 infection for whom it is otherwise not possible to construct a suppressive anti-viral regimen.

The Group reviewed the clinical and economic evidence in detail and the outputs of commercial negotiations.

The Drugs Group acknowledged that patients with MDR HIV-1 have very few treatment options and that there is a need for new classes of ARV drugs which are capable of providing potent, durable antiviral activity against MDR viruses. The Group reviewed the pivotal evidence from BRIGHTE, a Phase III, partially-randomised, international, double-blind, placebo-controlled study, conducted in 371 heavily-treatment experienced HIV-1 infected subjects with multi-class resistance. 272 subjects received either blinded Fostemsavir, 600 mg twice daily (n= 203), or placebo (n= 69), in addition to their current failing regimen, for 8 days of functional monotherapy. The primary endpoint analysis, based on the adjusted mean decline in HIV-1 RNA from Day 1 at Day 8 in the Randomised Cohort, demonstrated superiority of Fostemsavir to placebo (0.79 vs. 0.17 $\log_{10}$decline, respectively; $p<0.0001$, Intent To Treat-Exposed [ITT-E] population).

The Group noted the uncertainty surrounding eligible patient estimates and the consequent potential budget impact. The Drugs Group unanimously recommended hospital pricing approval of Fostemsavir (Rukobia®) when taking into consideration the unmet need in this cohort of patients and the commercial offer [redacted]. The Group's recommendation is subject to the development of a robust HSE clinical stewardship programme.

iv. 23022 Amivantamab (Rybrevant®) for NSCLC (NCPE HTA ID: 22004)

The Drugs Group considered Amivantamab (Rybrevant®) as monotherapy indicated for treatment of adult patients with advanced non-small cell lung cancer (NSCLC) with activating epidermal growth factor receptor (EGFR) Exon 20 insertion mutations, after failure of platinum-based therapy.

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 Drugs Group acknowledged the high mortality associated with NSCLC as well as the fact that a high proportion of patients experience severe morbidity as a result of local and metastatic spread of disease. The pivotal trial supporting marketing authorisation is the CHRYSALIS study (ṅ=114), a phase Ib/II, single arm, open-label study conducted to assess the safety and efficacy of Amivantamab in patients with locally advanced or metastatic NSCLC who had EGFR Exon 20 insertion mutations & whose disease had progressed on or after platinum-based chemotherapy. The primary efficacy endpoint was investigator-assessed overall response rate (ORR), defined as confirmed complete response (CR) or partial response (PR) based on RECIST v1.1. In addition, the primary endpoint was assessed by a blinded independent central review (BICR). ORR by investigator assessment was 36.8% (95% CI: 28%, 46.4%) with a 0% CR rate & median Duration of Response (DOR) was 12.5 months (95% CI: 6.5,16.1). ORR and DOR results by investigator assessment were consistent with those reported by BICR assessment.

Amivantamab is associated with very high drug acquisition costs with an estimated total cost per patient, per treatment course of €116,290 (including VAT) and ICERs at list price ranging from €150,242/QALY (Applicant base case, Amivantamab vs Physician's choice) to €183,181/QALY (NCPE adjusted base case, Amivantamab vs Physician's choice), which far exceed conventional willingness to pay thresholds.

The Drugs Group noted the uncertainties regarding the pivotal study, including the lack of comparator and the descriptive nature of the survival outcomes. The impact of the commercial offer submitted by the applicant company was considered by the Group to be of insufficient magnitude to support a positive recommendation. The Drugs Group unanimously did not support reimbursement of Amivantamab on the basis of the available clinical evidence, the considerable drug budget impact and the data available indicating that Amivantamab is not a cost-effective use of resources.

v. 23023 House Dust Mite (HDM) extract (Acarizax®) for adult patients (18 to 65 years) with house dust mite allergic asthma (NCPE HTA ID: 20016)

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

5. AOB

The Group reviewed the process and procedures in place for clinicians submitting representations for applications. This process is to be published online by the HSE CPU.

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
Clare Mac Gabhann	Director of Nursing and Midwifery (Prescribing)	In attendance
Position vacant	Mental Health Division (Consultant Psychiatrist)	Position vacant
Dr Cliona McGovern	Public Interest Member / Ethicist	In attendance
Mr Michael Power	Public Interest Member	Apologies received
Dr Anne Dee	Specialist in Public Health Medicine	Apologies received
Catherine Clarke	Strategy & Planning – Unscheduled Care (Assistant National Director)	Apologies received
Prof Ellen Crushell	Consultant in Inherited Metabolic Disorders	In attendance
Dr Lisa Cogan	Consultant in Medicine for the Elderly, Medical Director, Royal Hospital Donnybrook	Apologies received

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