HSE Drugs Group – October 2023 Minutes

Meeting 2023.09: Tuesday 17th October 2023, 14.00 – 16.30

Via videoconference

1. Draft Minutes for Consideration

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

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

i. Sacituzumab govitecan (Trodelvy®) for the treatment of metastatic triple-negative breast cancer (mTNBC) was considered by the Drugs Group in August 2023. The applicant (Gilead) submitted a revised commercial offer which was considered by the Drugs Group at the October 2023 meeting. The Group maintained its August 2023 position, that a positive reimbursement recommendation can be progressed, [redacted]

ii. Dostarlimab (Jemperli®) for recurrent or advanced endometrial cancer (dMMR/MSI-H subtype) was considered by the Drugs Group in August 2023. The applicant (GSK) submitted a revised commercial offer which was considered by the Drugs Group at the October 2023 meeting. The Group maintained its August 2023 position, that a positive reimbursement recommendation can be progressed, subject to the condition of [redacted]

iii. Cefiderocol (Fetcroja®) for infections due to aerobic Gram-negative organisms in adults with limited treatment options was considered by the Drugs Group in April 2023. The Drugs Group were notified that a revised commercial offering had been received into the HSE CPU. The Group agreed that this application should be included, and the offering further considered, at November 2023 Drugs Group meeting.

3. Declaration of Interests / Nil Interest

None declared

4. Medicines for Consideration

i. 20001 Darvadstrocel (Alofisel®) for the treatment of complex perianal fistulas in Crohn's Disease

The Drugs Group considered Darvadstrocel (Alofisel®) for the treatment of complex perianal fistulas in adult patients with non-active/mildly active luminal Crohn's disease, when fistulas have shown an inadequate response to at least one conventional or biologic therapy. At the September 2022 Drugs Group meeting it was agreed that Darvadstrocel (Alofisel®) be referred to the Rare Diseases Technology Review Committee (RDTRC) to assist in the Group's deliberations of this novel stem cell therapy. Following completion of the RDTRC processes, the Drugs Group were provided with the statement from the RDTRC for review, in addition to a draft Darvadstrocel HSE prescribing guideline. The totality of clinical and economic evidence for Darvadstrocel was comprehensively and extensively reviewed by the Drugs Group, in conjunction with the outputs from the RDTRC, at the October 2023 meeting.

[redacted]

The applicant (Takeda) communicated to the HSE CPU on the 18th of October 2023 that the Phase 3 ADMIRE-CD II study, assessing the efficacy and safety of Alofisel® (Darvadstrocel) for the treatment of complex Crohn's Perianal Fistulas (CPF), did not meet its primary endpoint of combined remission at 24 weeks. Takeda requested that the application for Darvadstrocel be paused until further information became available that could be provided to the HSE.

ii. 23024 Elexacaftor/Ivacaftor/Tezacaftor (Kaftrio®) for cystic fibrosis 2-5 years with a F/MF genotype or F/other genotype (NCPE HTA ID: 23036)

The Drugs Group considered Kaftrio® (Elexacaftor/Tezacaftor/Ivacaftor) indicated in a combination regimen with Kalydeco® (Ivacaftor) for the treatment of cystic fibrosis (CF) in patients aged 2 to 5 years who are heterozygous for the F508del mutation and either a minimal function (MF) mutation, or an unknown mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.

The Drugs Group acknowledged that CF is an autosomal recessive disease with serious, chronically debilitating morbidities and high premature mortality, and at present, there is no cure.

The Group reviewed the clinical efficacy data from one pivotal clinical trial which investigated use of Kaftrio® plus Ivacaftor in CF patients aged 2 to 5 years with the F508del mutation and a minimal function mutation (F/MF genotype). Analysis of pharmacokinetic data from 18 children enrolled in part A confirmed the appropriateness of the part B dosing regimen. In part B, 75 children (F508del/minimal function genotypes, n= 52; F508del/F508del genotype, n= 23) were enrolled and dosed. Children weighing <14 kg (on Day 1) received ELX 80 mg once daily (OD), TEZ 40 mg OD, and IVA 60 mg each morning and 59.5 mg each evening; children weighing ≥14 kg received ELX 100 mg OD, TEZ 50 mg OD, and IVA 75 mg every 12 hours. The primary endpoint of VX20-445-111 (Study 111) evaluated safety and tolerability of Kaftrio®. With regard to key secondary endpoints, Kaftrio® demonstrated improvements in CFTR function (as measured by changes in sweat chloride levels) and lung function (as measured by $LCI_{2.5}$) from baseline through to Week 24. A reduction of 57.5% was noted in mean SwCl levels, while a reduction of 9.9% was noted for mean $LCI_{2.5}$.

The Drugs Group unanimously recommended reimbursement, acknowledging the unmet need and that a price reduction [redacted] The Drugs Group however also acknowledged that Vertex CFTR modulators are high cost medicines and this positive recommendation had a notable opportunity cost attached to it.

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

The Drugs Group considered House Dust Mite Extract (Acarizax®) indicated in adult patients (18-65 years) diagnosed by clinical history and a positive test of house dust mite sensitisation (skin prick test and/or specific IgE) with house dust mite allergic asthma not well controlled by inhaled corticosteroids and associated with mild to severe house dust mite allergic rhinitis.

The Drugs Group reviewed the entirety of the available clinical and economic evidence, the outputs of commercial negotiations and also took into account a Patient Group Submission from the Asthma Society of Ireland.

The Group reviewed the evidence from the pivotal phase III, randomised, double-blind, placebo-controlled study (MITRA, MT-04), including 834 adults with House Dust Mite allergic asthma not well-controlled by daily use of inhaled corticosteroid (ICS). Subjects were randomised 1:1:1 to 7-12 months treatment with 12 SQ-HDM, 6 SQ-HDM or placebo in addition to ICS and short-acting beta-agonist prior to ICS reduction. Efficacy was assessed by time to first moderate or severe asthma exacerbation under ICS reduction over the last 6 months of 13-18 months of treatment. 12 SQ-HDM significantly reduced the risk of a moderate or severe asthma exacerbation compared with placebo in the full analysis set with multiple imputations (59/282 (21% vs 83/277 (30%); hazard ratio [HR]: 0.69 [95% CI, 0.50-0.96], P = 0.027).

The Group noted that budget impact estimates may be underestimated as the rate of testing for HDM sensitisation and proportion of patients to be treated are subject to considerable uncertainty. The Group also noted the considerable uncertainty associated with the magnitude of additional clinical benefit to be gained from the introduction of Acarizax® given the lack of long-term evidence and the marginal incremental QALY gain demonstrated in the cost effectiveness analysis reported by both the applicant and the NCPE. On the basis of the entirety of the evidence presented, and outstanding uncertainty, the Drugs Group unanimously recommended against reimbursement of Acarizax® in this indication.

iv. 23025 Enfortumab vedotin (Padcev®) for urothelial cancer (NCPE HTA ID: 22024)

The Drugs Group considered Enfortumab Vedotin (Padcev®) for the treatment of adult patients with locally advanced or metastatic urothelial cancer (UC) who have previously received a platinum-containing chemotherapy and a programmed death receptor-1 or programmed death-ligand 1 inhibitor.

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 UC is an aggressive malignancy with untreated locally advanced or metastatic UC associated with a median survival time rarely exceeding 4-6 months. It was also noted that once patients are beyond platinum and immunotherapy, treatment choices are scarce.

The efficacy of Enfortumab Vedotin (EV) was evaluated in study EV-301, an open-label, randomised, phase III, multicentre study that enrolled 608 patients with locally advanced or metastatic UC who previously received a platinum-containing chemotherapy and a PD-1 or PD-L1 inhibitor. The primary endpoint of the study was Overall Survival (OS) and secondary endpoints included Progression Free Survival (PFS) and Objective Response Rate (ORR). OS in the EV arm showed statistical superiority over chemotherapy [HR for OS 0.70 (95% CI 0.56, 0.89), p-value 0.00142]. K-M (Kaplan–Meier) estimates of median OS are 12.9 months in the EV arm and 9.0 in the chemotherapy arm. At 71% of PFS events, [HR for PFS was 0.62 (95% CI 0.51, 0.75), p-value <0.00001]. K-M estimates of median PFS were 5.6 months in the EV arm and 3.7 in the chemotherapy arm. Confirmed ORR rate was 41% in the EV arm (n=288) and 18% in the chemo arm (n=296).

At list price the ICER for Enfortumab vedotin ranged from €161,060/QALY (applicant base case) to €195,334/QALY (under NCPE preferred assumptions) versus taxane based chemotherapy. The applicant (Astellas) offered a [redacted] on the list price (inclusive of the mandatory IPHA rebate). The ICERs resultantly decreased to [redacted]/QALY (applicant base case) and [redacted]/QALY (NCPE preferred assumptions). The Drugs Group recognised the substantial improvement in cost-effectiveness and by majority voted in favour of reimbursement.

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

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

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)	N/A
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)	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	Apologies received

*Parts of meeting and some voting not attended

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