HSE Drugs Group – March 2023 Minutes

Meeting 2023.03: Tuesday 14th March 2023, 14.00 – 16.30

Via videoconference

1. Draft Minutes for Consideration

The minutes of the February 2023 meeting were considered and approved. December 2022 minutes required an update as a minor error was noted prior to online publication, and that minor amendment was also approved. The December 2022 minutes will be updated accordingly and published in due course

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 meeting

i. An update on items previously considered by the Drugs Group was provided. The positive recommendations for Apalutamide (for mHSPC) from the October 2022 meeting, Mogamulizumab (for mycosis fungoides or Sézary syndrome) from the January 2023 meeting, Risdiplam (for 5q SMA), Niraparib (for ovarian cancer), Pembrolizumab (for MSI-H /dMMR colorectal cancer), Nivolumab + Ipilimumab (for mesothelioma) and Andexanet alfa (for anticoagulation reversal) from the February 2023 meeting had been progressed to the HSE Executive Management Team (EMT) for consideration. Following the Drugs Group meeting in December 2022, negative recommendations for Ravulizumab (2 applications) were also progressed to the HSE EMT for consideration.

ii. A recently published report prepared by Mazars, examining the governance arrangements around the HSE's drug reimbursement process had been shared with the Drugs Group members, which was noted.

iii. 

4. Declaration of Interests / Nil Interest

None declared

5. Medicines for Consideration

i. 22031 Atidarsagene autotemcel (Libmeldy®) for metachromatic leukodystrophy (MLD)

The Drugs Group considered Atidarsagene autotemcel (Libmeldy®) indicated for the treatment of metachromatic leukodystrophy (MLD) characterized by biallelic mutations in the arylsulfatase A (ARSA) gene leading to a reduction of the ARSA enzymatic activity in children with late infantile (LI) or early juvenile (EJ) forms, without clinical manifestations of the disease, and in children with the early juvenile form, with early clinical manifestations of the disease, who still have the ability to walk independently and before the onset of cognitive decline.

At the December 2022 meeting the Drugs Group were in favour of hospital pricing approval for this once off gene therapy, if the specific terms set out in a proposed joint mandate were to emerge. This positive recommendation was conditional on the applicant company (Orchard Therapeutics) agreeing to these terms, which would be sought by the HSE in conjunction with the equivalent Dutch and Belgian health authorities via the Beneluxa Initiative. The terms were based on the recommendations arising from the HTA report conducted on a collaborative basis by HTA bodies in Ireland, the Netherlands and Belgium.

The mandate was not achieved by the Beneluxa Initiative through joint negotiations with Orchard Therapeutics, with negotiations having to be concluded in line with the timeframe permitted for same

[redacted]

The Drugs Group reviewed the entirety of the available clinical and economic evidence and also took into account a Patient Group Submission during deliberations at the March 2023 meeting.
The Group acknowledged that metachromatic leukodystrophy (MLD) is a rare inherited lysosomal storage disease for which there is currently no curative treatment and that in the absence of treatment able to modify the disease pathophysiology, the disease inevitably ends in decerebrated state and eventually death.

The Group reviewed the clinical efficacy which was primarily based on the integrated analysis of results from 29 early-onset MLD patients treated with Libmeldy® prepared as a fresh (non-cryopreserved) formulation. These results were generated in 20 patients treated in the Registrational Study (Study 201222 - an open-label, non-randomized, single-arm safety and efficacy clinical trial) with a median duration of post-treatment follow-up of 4.0 years (range: 0.6 to 7.5 years) and 9 patients treated in the context of 3 expanded access programs with a median follow-up of 1.5 years (range: 0.99 years to 2.72 years).

[redacted]

ii. 23003 Cenobamate for epilepsy

The Drugs Group considered Cenobamate (Ontozry®) for the adjunctive treatment of focal-onset seizures with or without secondary generalisation in adult patients with epilepsy who have not been adequately controlled despite a history of treatment with at least two anti-epileptic medicinal products.
The Drugs Group reviewed the entirety of the available clinical and economic evidence and also took into account a Patient Group Submission from Epilepsy Ireland during deliberations.

The Group reviewed the clinical evidence from study C017, a Phase II, multi-centre, randomised, double-blind, placebo-controlled trial in adult patients with focal-onset epilepsy who have not been adequately controlled despite a history of treatment with anti-epileptic drugs. The study compared doses of Cenobamate 100 mg/day, 200 mg/day and 400 mg/day with placebo, on top of standard of care. The responder rate (as primary endpoint: responder defined as at least 50% Focal Onset Seizure frequency reduction) was 40.2% (41/102) for 100mg Cenobamate, 56.1% (55/98) for 200mg Cenobamate and 64.2% (61/95) for 400mg Cenobamate as compared to 25.5% (26/102) for placebo. In study C017, 4 of 102 (3.9%) patients in the Cenobamate 100 mg/day group, 11 of 98 (11.2%) patients in the Cenobamate 200 mg/day group, 20 of 95 (21.1%) patients in the Cenobamate 400 mg/day group and 1 of 102 (1%) of patients in the placebo group obtained seizure freedom (100% reduction in seizures) during the 12-week fixed-dose phase.

The Group recognised that Cenobamate, an orally administered novel tetrazole-derived carbamate, represented an alternative treatment option for patients with drug resistant epilepsy (DRE). The Drugs Group unanimously recommended reimbursement of Cenobamate, noting the unmet need, the totality of the clinical evidence available and the cost-effectiveness evidence, as reported by the National Centre for Pharmacoeconomics (NCPE), in which Cenobamate was demonstrated to be more effective and less costly than all comparators.

iii. 23004 Elexcaftor/Ivacaftor/Tezacaftor (Kaftrio®) for cystic fibrosis

The Drugs Group considered Ivacaftor/Tezacaftor/Elexacaftor (Kaftrio®) in a combination regimen with Ivacaftor (Kalydeco®) in cystic fibrosis patients aged 6 -11 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 Group previously considered a commercial offering from Vertex, for this application, at the June 2022 meeting, at which point the group concluded they would not be able to provide a recommendation to the HSE EMT in the absence of a full Health Technology Assessment that would assess the clinical effectiveness and cost-effectiveness compared with the current standard of care, as had been advised by the National Centre for Pharmacoeconomics. The Drugs Group comprehensively reviewed the entirety of the available clinical and economic evidence and also took into account a Patient Group Submission from Cystic Fibrosis Ireland during deliberations at the March 2023 meeting. The Group noted that the commercial offering and the Health Technology Assessment output were the result of several months of engagement by the HSE and the NCPE with Vertex on this application.

The clinical evidence supporting this application includes four clinical trials which investigated the use of Kaftrio® plus Ivacaftor in CF patients aged 6 to 11 years with the F508del mutation and a minimal function mutation (F/MF genotype). The four trials include two completed phase 3/phase 3b studies and two ongoing open-label extension (OLE) studies i.e. GALILEO and GALILEO OLE in addition to the AURORA 6-11 and AURORA 6-11 OLE trials. The GALILEO trial was a randomised, double-blind, placebo-controlled phase 3b study designed to evaluate the efficacy and safety of Kaftrio® plus Ivacaftor in children 6 through 11 years of age with the F/MF genotype. Children were randomised to receive either Kaftrio® plus Ivacaftor (n=60) or placebo (n=61) during a 24 week treatment period. The primary endpoint was absolute change in lung clearance $index_{2.5}$ ($LCI_{2.5}$) from baseline through week 24. Children given Kaftrio® plus Ivacaftor had a mean decrease in lung clearance $index_{2.5}$ of 2.29 units as compared with 0.02 units in the placebo group (between group difference, -2.26 units; 95% confidence interval (CI), -2.71 to -1.81:$p<0.0001$). Kaftrio® plus Ivacaftor treatment also resulted in clinically meaningful improvements in the secondary endpoints of ppFEV1, sweat chloride concentration and CFQ-R respiratory domain score. The AURORA 6-11 trial was a 24 week, open-label phase 3 study including 66 children where the safety and pharmacokinetics of Kaftrio® plus Ivacaftor was studied. Kaftrio® in combination with Ivacaftor improved the ppFEV1 by 10.2% (95% CI, 7.9% to 12.6%) by week 24. The CFQ-R respiratory domain score increased by 7 points (95% CI, 4.7 to 9.2 points) and sweat chloride fell by 60.9 mmol/L.

The Drugs Group acknowledged that Vertex CFTR modulators are high cost medicines. A deterministic analysis of the cost-effectiveness of Kaftrio® plus Ivacaftor (at list price) vs Best supportive care determined that the base case incremental cost-effectiveness ratio (ICER) was €263,202/QALY. The price – ICER relationship indicated that a [redacted] price reduction applied to both Kaftrio® and Ivacaftor (Kalydeco®) was required to produce an ICER of approximately €45,000/QALY. The group noted a price reduction [redacted] has been achieved [redacted] The Drugs Group unanimously recommended reimbursement, acknowledging the unmet need and the substantial improvement in cost-effectiveness when making its recommendation.

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

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

v. 23005 Nivolumab + Ipilimumab for metastatic colorectal cancer

There was insufficient time for the Drugs Group to conclude deliberations on this application. This will be carried forward to the April 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	In attendance
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

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