HSE Drugs Group – December 2022 Minutes

Meeting 2022.11: Tuesday 6th December 2022, 14:00-16:00
Meeting 2022.12: Tuesday 13th December 2022, 14:00-16:00

Via videoconference

1. Draft Minutes for Consideration

The minutes of the November 2022 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 meeting

Positive recommendations for Brentuximab Vedotin license extensions (3 applications) were progressed to the HSE Executive Management Team as the applicant company enhanced commercial offer was deemed satisfactory in accordance with the Drugs Group requirements to support these applications.

The Drugs Group were notified of an indicative number of 2022 approvals and the finalised number is to be reported formally to the Group in Q1 2023. The Group were made aware of an increase in the volume of applications as well an increase in the number of approvals compared with 2021.

4. Declaration of Interests / Nil Interest

None declared.

5. Medicines for Consideration

i. 22003 Olaparib for metastatic castration resistant prostate cancer

Olaparib for metastatic castration resistant prostate cancer (mCRPC) was previously considered by the Drugs Group in February 2022, where the Drugs Group noted that there was a high degree of uncertainty in relation to the generalisability (to Irish clinical practice) of the available clinical evidence, in the main due to a lack of direct comparative evidence to treatment with taxanes. The applicant (AstraZeneca) was therefore requested to provide further supporting evidence, the entirety of which was submitted but ultimately not considered robust by the Group to be informative for the decision. The Group discussed the unmet need, a relatively modest overall drug budget impact, the totality of the clinical evidence available and the strong support from the clinical community in relation to the benefits offered by having Olaparib available for a select cohort of patients with mCRPC. The majority decision of the Group was to recommend reimbursement of Olaparib within its licensed indication on that basis.

ii. 22029 Encorafenib for metastatic colorectal cancer

The Drugs Group considered Encorafenib (Braftovi®) in combination with Cetuximab, for the treatment of adult patients with metastatic colorectal cancer (CRC) with a BRAF V600E mutation, who have received prior systemic therapy. The Drugs Group noted that BRAF V600-mutant CRC is considered a distinct subtype of CRC that has unique clinical characteristics and is associated with a worse prognosis, with a negative impact on both overall survival (OS) and progression-free survival

(PFS). 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). The key evidence informing this indication came from the PIII BEACON CRC trial. The trial was a three-arm trial consisting of a triplet arm (Encorafenib in combination with Binimetinib and Cetuximab) versus a doublet arm (Encorafenib and Cetuximab) versus chemotherapy arm (FOLFIRI +Cetuximab or Irinotecan +Cetuximab). The doublet arm vs chemotherapy arm is of interest for this indication. The study demonstrated a modest improvement in overall survival (OS) of 9.3 months in the doublet arm vs 5.88 months in the chemotherapy arm, with a HR of 0.61 ($p<0.0001$). Taking account both the perspective of the applicant and the NCPE RG the impact of the commercial offering [redacted] The Drugs Group in the majority were unable to recommend in favour of reimbursement given the challenges with cost-effectiveness, overall modest clinical benefits alongside the considerable proposed budget impact.

iii. 22030 Trifluridine / Tipiracil for metastatic gastric cancer

The Drugs Group considered Trifluridine + Tipiracil (Lonsurf®) indicated as monotherapy for the treatment of adult patients with metastatic gastric cancer including adenocarcinoma of the gastroesophageal junction, who have been previously treated with at least two prior systemic treatment regimens for advanced disease. The Drugs Group recognised that there are limited alternative treatment options at this stage. The Group reviewed the clinical and economic evidence in detail. The supporting evidence for this indication is primarily the phase III TAGS study which evaluated the efficacy and safety of Lonsurf® or placebo with best supportive care (BSC) in patients with previously treated (at least two prior lines) advanced metastatic gastric cancer. The primary endpoint was overall survival (OS) and secondary endpoints were progression free survival (PFS), overall response rate (ORR), disease control rate (DCR) and quality of life. The study met its primary endpoint, and showed modest improvement in survival with a median OS of 5.7 months for Lonsurf® vs 3.6 months for placebo, with a HR of 0.69 (2-sided p-value 0.0006). There was also a statistically significant improvement in PFS reported, although no real difference in the reported median PFS (2 months vs 1.8 months). The Drugs Group agreed unanimously that it could not support reimbursement of Trifluridine + Tipiracil at the confidential price proposed. This was due to the modest magnitude of clinical benefit overall and the likelihood that this treatment would be challenged to demonstrate cost-effectiveness (vs BSC) at conventional willingness to pay thresholds based on the price proposed and current supportive evidence available.

iv. 21006a Ravulizumab for paroxysmal nocturnal haemoglobinuria (PNH)

The Drugs Group did not recommend reimbursement of Ravulizumab for the treatment of adults with PNH for either patients with haemolysis with clinical symptom(s) indicative of high disease activity or in patients who are clinically stable after having been treated with Eculizumab for at least the past 6 months. There is a high degree of uncertainty in the associated cost-effectiveness (vs Eculizumab) due to the imminent availability of biosimilar Eculizumab. The commercial offer submitted by the applicant was considered of insufficient magnitude to overcome this uncertainty. The Drugs Group considered the market value for complement inhibitors to be attractive and therefore there is potential for significant efficiencies to be gained if there is competition through biosimilar developments. These efficiencies were considered to have the potential to be greater than [redacted]. In making its recommendation the Drugs Group also acknowledged the potential benefits of Ravulizumab through longer intervals between administrations wouldn't be realised, but formed a view that this was insufficient in and of itself to support reimbursement at this point given the very high cost of treatment, very high budget impact (based on a market with biosimilars) and very high opportunity costs (based on a market with biosimilars).

v. 21006b Ravulizumab for atypical haemolytic uraemic syndrome (aHUS)

The Drugs Group did not recommend reimbursement of Ravulizumab for the treatment of patients with a body weight of ≥10 kg with aHUS who are complement inhibitor treatment-naïve or have received Eculizumab for at least 3 months and have evidence of response to Eculizumab. There is a high degree of uncertainty in the associated cost-effectiveness (vs Eculizumab) due to the imminent availability of biosimilar Eculizumab. The commercial offer submitted by the applicant was considered of insufficient magnitude to overcome this uncertainty. The Drugs Group considered the market value for complement inhibitors to be attractive and therefore there is potential for significant efficiencies to be gained if there is competition through biosimilar developments. These efficiencies were considered to have the potential to be greater than [redacted]. In making its recommendation the Drugs Group also acknowledged the potential benefits of Ravulizumab through longer intervals between administrations wouldn't be realised, but formed a view that this was insufficient in and of itself to support reimbursement at this point given the very high cost of treatment, very high budget impact (based on a market with biosimilars) and very high opportunity costs (based on a market with biosimilars).

vi. 22013 Larotrectinib for solid tumours with a NTRK gene fusion

The Drugs Group considered Larotrectinib (Vitrakvi®) as monotherapy for the treatment of adult and paediatric patients with solid tumours that display a Neurotrophic Tyrosine Receptor Kinase (NTRK) gene fusion, who have a disease that is locally advanced, metastatic or where surgical resection is likely to result in severe morbidity, and who have no satisfactory treatment options. The totality of clinical and economic evidence for Larotrectinib was comprehensively reviewed by the Drugs Group in May 2022. After an extensive discussion the Drugs Group requested further information be brought forward to assist it in making its final recommendation, namely an enhanced commercial offering requiring further engagement with the applicant company and a managed access protocol, which was duly requested from the HSE Medicines Management Programme and shared (in draft) in full with the Drugs Group in December 2022. On reviewing the requested further information the Drugs Group considered it sufficient to support a positive recommendation for this application.

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

The Drugs Group considered the clinical and cost-effectiveness evidence available for Atidarsagene autotemcel along with a completed Patient Group submission received during the HTA process. 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 is conditional on the applicant company (Orchard Therapeutics) agreeing to these terms, which will 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.

viii. 22032 Risdiplam for 5q spinal muscular atrophy (SMA)

Prior to the availability of disease modifying treatments, management of SMA consisted mainly of best supportive care (BSC) (i.e. supportive, rehabilitative and palliative care to treat or prevent complications of muscle weakness and maintain quality of life). Nusinersen and onasemnogene abeparovec are disease modifying treatments. Nusinersen is reimbursed, in Ireland, for the treatment of SMA Type I, II and III in patients aged under 18 years. Onasemnogene abeparovec is reimbursed, in Ireland, for patients with a confirmed diagnosis of 5q SMA with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of SMA Type I, or a confirmed diagnosis of pre-symptomatic 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene. Risdiplam is the first orally administered targeted therapy licensed for the management of SMA. The applicant (Roche)

applied for reimbursement in accordance with the licensed indication. The Drugs Group reviewed the entirety of the available clinical and economic evidence and also took into account a Patient Group Submission from SMA Ireland during deliberations. The Group noted the advantage of having an oral treatment available for patients with SMA, noting some of the complications of the condition (e.g. scoliosis) can preclude eligibility for the more invasive treatment option of Nusinersen. On the basis of the value of the commercial offer submitted by Roche being applicable to a restricted population (Type I, II and III SMA <18 years) the Drugs Group were willing to progress a positive recommendation conditional on a Managed Access Protocol being put in place to ensure appropriate prescribing of this high cost medicine. This recommendation took into account reported cost-effectiveness versus relevant comparators (that are subject to confidential discounts) and the current limitations in the available evidence for efficacy when initiating targeted treatments in adults with SMA.

ix. 22033 Vericiguat for long-term heart failure with reduced ejection fraction

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

x. 22034 Mogamulizumab for mycosis fungoides (MF) or Sézary syndrome (SS)

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

6. AOB

Appendix 1: Members Present on Microsoft Teams

Member	Title	Attendance 06/12	Attendance 13/12
Prof. Áine Carroll	Chair, Medical Consultant	In attendance	In attendance
Mr Shaun Flanagan	Primary Care Reimbursement Service (Assistant National Director)	In attendance	In attendance
Ms Aoife Kirwan	Public Interest Member	Apologies received	Apologies received
Dr David Hanlon	National Clinical Advisor and Group Lead Primary Care (General Practitioner)	In attendance	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	In attendance
Dr Philip Crowley	National Director for Quality Improvement (Medical Doctor)	In attendance	Apologies received
Dr Valerie Walshe	Office of the Chief Financial Officer (Economist, PhD)	In attendance	In attendance
Post Vacant	Office of Nursing & Midwifery Services (Director of Nursing)	n/a	n/a
Dr Roy Browne	Mental Health Division (Consultant Psychiatrist)	Apologies received	Apologies received
Dr Cliona McGovern	Public Interest Member / Ethicist	Apologies received	In attendance
Mr Michael Power	Public Interest Member	In attendance	Apologies received
Dr Anne Dee	Specialist in Public Health Medicine	In attendance	In attendance
Post Vacant	Acute Operations Division (Assistant National Director)	n/a	n/a
Prof Ellen Crushell	Consultant in Inherited Metabolic Disorders	In attendance	In attendance
Dr Lisa Cogan	Consultant in Medicine for the Elderly, Medical Director, Royal Hospital Donnybrook	In attendance	In attendance

In attendance (non-voting):
Dr Michael Barry (NCPE) on 6th December and 13th December 2022

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