HSE Drugs Group – May 2022 Minutes

Meeting 2022.05: Tuesday 10th May 2022, 14.00 – 16.00

Via videoconference

1. Draft Minutes for Consideration

The minutes of the April 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 meetings

The April 2022 Drugs Group recommendations had been considered and subsequently approved by the HSE Executive Management Team (EMT).

The Drugs Group previously considered Obeticholic acid (Ocaliva®) for the treatment of primary biliary cholangitis in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA or as monotherapy in adults unable to tolerate UDCA at their December 2019 meeting. Obeticholic acid received a qualified positive recommendation from the Drugs Group on that occasion. The applicant submitted a revised commercial proposal that met the conditions required by the Drugs Group to progress a positive recommendation to the HSE EMT. The HSE EMT subsequently approved Obeticholic acid for this indication subject to the development of a managed access programme.

4. Declaration of Interests / Nil Interest

No potential conflicts were raised.

5. Miscellaneous

In advance of the Drugs Group's consideration of Larotrectinib (Vitrakvi®), the Chair invited Ms. Caroline Walsh from the National Centre for Pharmacoeconomics (NCPE) to provide members with an overview of tumour-agnostic therapies from the perspective of the NCPE as a Health Technology Assessment (HTA) agency. One of the key concepts presented included the challenges associated with basket trials, which typically provide single-arm, phase I/II trial data for a surrogate outcome such as overall response rate, as opposed to a survival outcome, as the primary endpoint. The challenges of working with the clinical evidence for tumour-agnostic therapies and the uncertainties in modelling treatment effectiveness were outlined and included: the frequently ongoing nature of basket trials at the point of Health Technology Assessment, the multiple datasets with changing patient numbers, immature time-to-event data, assumptions of homogeneity of treatment response, and naïve indirect treatment comparisons. Approaches to addressing some of the uncertainties associated with tumour-agnostic therapies were also presented to the Group. A robust discussion ensued in which the Group acknowledged the inherent challenges and uncertainties in considering reimbursement of these therapies. Ms. Caroline Walsh and Professor Michael Barry of the NCPE addressed a number of queries raised by the Drugs Group members and were duly thanked by the Chair and Group for their valuable insight on tumour-agnostic therapies in advance of the first such therapy being considered for reimbursement by the Group.

6. Medicines for Consideration

i. 22012 Pegylated liposomal Irinotecan for pancreatic adenocarcinoma

The Drugs Group considered pegylated liposomal Irinotecan (Onivyde® Pegylated Liposomal) for the treatment of metastatic adenocarcinoma of the pancreas, in combination with 5-fluorouracil (5-FU) and Leucovorin (LV), in adult patients who have progressed following Gemcitabine based therapy. The very poor prognosis associated with pancreatic adenocarcinoma and the lack of therapeutic developments in this space was acknowledged by the Group. The Group reviewed the evidence from the pivotal NAPOLI–1 study, noting that a median overall survival benefit of 2 months was observed for the Onivyde® Pegylated Liposomal +5-FU/LV arm compared to the 5-FU/LV arm, based on the final overall survival analysis. In the limited number of patients with prior exposure to non-liposomal Irinotecan, benefit of Onivyde® Pegylated Liposomal has not been demonstrated. The Drugs Group noted that 5-FU/LV, the comparator in the trial, is not the routine standard of care in Ireland and may be inferior to current clinical practice. The Group considered that mFOLFOX would have been a preferable comparator arm. The Group acknowledged that there was uncertainty as to whether the very modest treatment benefit seen in NAPOLI-1 was generalisable to clinical practice in Ireland.

Onivyde® Pegylated Liposomal was considered by the Group to be an expensive medicine with incremental cost-effectiveness ratios (ICERs) versus both 5-FU/LV and mFOLFOX far exceeding conventional willingness to pay thresholds under both the applicant and NCPE's base cases (in both the ITT and Irinotecan-naïve populations), when either list price or the confidential net price proposed by the applicant were reviewed. Following consideration of the unmet clinical need, the clinical evidence, the considerable cost-effectiveness estimates, and the significant budget impact of this treatment (notwithstanding the commercial offer), the Drugs Group unanimously agreed that it could not support reimbursement of Onivyde® Pegylated Liposomal.

ii. 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 and extensively reviewed by the Drugs Group, followed by a protracted discussion.

The Group noted that NTRK gene fusions are not specific to any organ and can occur in both adults and paediatric populations, across multiple tumour types. NTRK gene fusions have been identified at low frequencies in a wide range of commonly occurring tumours but are the defining genetic feature in some very rare tumours such as infantile fibrosarcoma. Larotrectinib represents a potential treatment option for locally advanced or metastatic malignant solid tumours after standard therapy or when there is no appropriate available therapy.

The Group reviewed and discussed the clinical evidence in detail, noting the impressive overall response rates in a generally late stage disease setting, and the substantial median decrease in tumour size in the pooled primary analysis set which suggested a positive Larotrectinib treatment effect. However, the Group considered there to be many uncertainties in the trial including the immaturity of data, the single-arm nature of the trials, and the small patient numbers enrolled in the trial which make it difficult to draw conclusions on homogeneity of possible effects between tumour types. The association between NTRK gene fusions and prognosis in terms of longer-term clinical outcomes such as overall survival have not yet been fully established.

The difficulties in modelling cost-effectiveness for tumour-agnostic therapies such as Larotrectinib were acknowledged by the Group. The deterministic incremental cost-effectiveness ratios (ICERs) generated under the applicant's corrected base case and the NCPE adjusted base case versus the pooled comparators ranged from €129,543/QALY to €163,864/QALY respectively. The Group noted that considerable uncertainty was associated with the NCPE adjusted base case ICER despite a number of preferred inputs to the model. The Group considered that while the commercial offer improved the cost-effectiveness estimates, the confidential net price did not adequately reflect the outstanding clinical and pharmacoeconomic uncertainty associated with Larotrectinib. The substantial investment required to fund Larotrectinib treatment was also recognised, with the cost of testing for NTRK gene fusions a further significant budgetary consideration. Following lengthy deliberations by the Drugs Group, it was agreed that an improved commercial offering be sought [redacted], in addition to the development of a managed access protocol for further review and deliberation by the Group, prior to a recommendation being issued for Larotrectinib.

iii. 22014 Brentuximab vedotin for CD30+ Hodgkin Lymphoma (HL) at increased risk of relapse or progression following autologous stem cell transplant (ASCT)

There was insufficient time for the Drugs Group to conclude deliberations on this application due to the complex deliberations for agenda item 22013. This will be carried forward to the June 2022 meeting.

iv. 22015 Brentuximab vedotin for previously untreated systemic anaplastic large cell lymphoma (sALCL)

There was insufficient time for the Drugs Group to conclude deliberations on this application due to the complex deliberations for agenda item 22013. This will be carried forward to the June 2022 meeting.

v. 22016 Brentuximab vedotin for CD30+ cutaneous T-cell lymphoma (CTCL)

There was insufficient time for the Drugs Group to conclude deliberations on this application due to the complex deliberations for agenda item 22013. This will be carried forward to the June 2022 meeting.

vi. 22017 Avelumab for urothelial carcinoma

There was insufficient time for the Drugs Group to conclude deliberations on this application due to the complex deliberations for agenda item 22013. This will be carried forward to the June 2022 meeting.

7. AOB

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 AnneMarie De Frein for Professor Risteárd Ó Laoide	Deputy Chief Pharmacist, National Cancer Control Programme for National Director of the National Cancer Control Programme (Medical Consultant)	In attendance (non-voting) 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
Ms Joan Donegan	Office of Nursing & Midwifery Services (Director of Nursing)	In attendance
Dr Roy Browne	Mental Health Division (Consultant Psychiatrist)	In attendance
Dr Cliona McGovern	Public Interest Member / Ethicist	In attendance
Mr Michael Power	Public Interest Member	Apologies received
Post Vacant	Health and Wellbeing Division (Public Health Physician)	n/a
Post Vacant	Acute Services 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	Apologies received

*Parts of meeting and voting not attended

In attendance (non-voting):
Ms Kate Mulvenna
Professor Michael Barry (NCPE)
Ms Caroline Walsh (NCPE)

Secretariat:
Fiona Mulligan, Chief II Pharmacist, CPU PCRS
Jennifer McCartan, Chief II Pharmacist, CPU PCRS
Mary Staunton, Chief II Pharmacist, CPU PCRS