HSE Drugs Group – November Minutes

Meeting 2018.10: Tuesday 13th November 2018, 14.00
Board Room, Unit 4A, The Dargan Building, Heuston South Quarter, Military Road, Kilmainham, D8

1. Draft Minutes for Consideration

The minutes of the meeting of the 9th and 23rd October 2018 were circulated late. It was agreed the draft minutes would be reviewed by member's offline and any changes would be approved at the next meeting.

2. Declaration of Interests / Nil Interest

No conflicts of interest arose.

3. Matters arising / Update on Medicines considered at previous meetings

CPU provided the members with an update in relation to items previously considered. CPU confirmed that the positive recommendations with SLT currently would amount to an estimated budget impact of €130m+ over 5 years.

4. Updates:

i. Rare Diseases TRC: the Drugs Group agreed a protocol whereby it would only refer Orphan Medicines to the RDTRC where it felt it had insufficient information available to support a positive recommendation.
ii. NCCP TRC: any recommendations in relation to specific medicines would be flagged as the medicines were being reviewed

5. Medicines for Consideration

i. 18023 Ocrelizumab for Multiple Sclerosis (RRMS & PPMS)

The Drugs Group recognised that there was an unmet need for market authorised therapies for PPMS but noted the company submission relied on imputed data and involved the modelling of relatively short term data out for many years and therefore the evidence around cost effectiveness was highly uncertain.

The Drugs Group unanimously agreed that it could not support funding of Ocrelizumab at the price proposed by Roche as it would result in a very large budget impact and significant opportunity costs.

The Drugs Group unanimously agreed that it would support funding of Ocrelizumab for PPMS if a commercial offering of a [redacted] emerged. Such a price reduction would reduce the significant impacts on other services that would arise from the funding of Ocrelizumab and would also open up the possibility that Ocrelizumab might be cost effective.

The Drugs Group noted that there was a wide range of therapies approved and funded for relapsing and remitting multiple sclerosis. The Drugs Group unanimously agreed that it could not support funding of Ocrelizumab for RRMS at the price proposed by Roche as it would result in a very large budget impact and significantly impact on other services.

The Drugs Group unanimously agreed that it would support funding of Ocrelizumab for RRMS if a commercial offering of a [redacted] emerged.

ii. 18024 Ataluren for Duchenne Muscular Dystrophy

The Drugs Group found the review of Ataluren to be very challenging. The Drugs Group reviewed in detail the two controlled trials (Study 007 and Study 020), the various extensions and a meta-analysis of both of these studies, real world evidence from the company registry (STRIDE) as well as pulmonary function evidence from STRIDE and Study 019. The Drugs Group noted the various comparisons to a historical untreated cohort (CINRG) and data submitted to PTC by an Irish expert in relation to historical loss of ambulation in Irish patients.

The Drugs Group review of the evidence noted that neither of the two double blind placebo controlled trials would be regarded as conventionally successful trials. However the European Medicines Agency (EMA) did approve a conditional marketing authorisation (which has been renewed on a number of occasions since then) on the back of Study 007.

The Drugs group noted information from the STRIDE Registry on age at loss of ambulation (data cut-off July 2018) recently provided. The Drugs Group noted that a further double-blind placebo controlled trial has been required by the EMA (due to report in 2021) but that trial is understood to be recruiting outside of both the EU (due to the commercial availability of Ataluren) and the USA.

Ataluren was an expensive oral medicine with a weight based dosing. The cost per quality adjusted life year (based on the company HTA submission in 2016 and the proposed commercial terms) would fall between [redacted]/QALY if assumptions applied in the HTA were accepted.

These estimates were predicated on the hypothesis that Ataluren was an effective medicine which would significantly delay loss of ambulation and delay loss of life. The robustness of that hypothesis and the exact magnitude of any such delay was uncertain due to the immaturity of the data available. The company had accepted that an additional HTA would not substantially change the cost effectiveness estimates.

The Drugs Group agreed the issue for consideration could be summarised by two questions which ultimately amounted to the same question from different perspectives:

- Was there (now) sufficient evidence available to support the reimbursement of Ataluren at a budget impact of [redacted] over 5 years in the context of an understanding that the medicine is not cost effective?

Or alternatively

- Was there sufficient uncertainty around any long term benefits of the medicine to deny access to the medicine to approximately 10 children (or less) in the context of a relatively modest and limited budget impact [redacted] over 5 years with little or no risk around increases in patient number and a medicine with a benign safety profile) even in the context of the poor value for money evidence.

The Drugs Group agreed these were very challenging questions to answer. The Group could not agree a consensus position and it progressed to a vote on Ataluren. By a single vote the majority supported reimbursement conditional on reimbursement ceasing once ambulation was lost i.e. the HSE not paying beyond loss of ambulation and the ongoing continued availability of all of the commercial terms offered.

iii. 18025 Pembrolizumab 1st Line Urothelial Carcinoma

The Drugs Group agreed that it could not make a recommendation without a full and robust budget impact assessment as there was too much uncertainty around the possible budget impact presented notwithstanding efforts to provide additional certainty around treatment duration.

iv. 18026 Ribociclib for Breast Cancer

The Drugs Group recommended in favour of Ribociclib on a cost minimisation basis i.e. no additional costs to accrue to the State from the use of Ribociclib over other relevant comparator(s).

v. 18027 Avelumab for Merkel Cell Carcinoma

Insufficient time was available to consider this medicine.

vi. 18028 Atezolizumab for 2nd Line NSCLC

The Drugs Group unanimously agreed that it could only support funding of Atezolizumab for 2nd line treatment of non-small cell lung cancer, if, on the basis of a cost minimisation approach versus the already approved and funded immunotherapy Nivolumab, Atezolizumab was demonstrated to be no more expensive than Nivolumab.

The applicant had not met the required threshold with its commercial offer.

vii. 18029 Mercaptamine for Cystinosis

Insufficient time was available to consider this medicine.

AOB

An induction meeting for new and existing members scheduled for 27th Nov was flagged.

Appendix 1: Members Present

Member	Title	13th Nov 2018
Prof. Áine Carroll	Chair, Medical Consultant	In attendance
Ms Anne Marie Hoey	Primary Care Reimbursement Service (Assistant National Director)	In attendance
Prof. Michael Barry	Medicines Management Programme / National Centre for Pharmacoeconomics (Clinical Director - Consultant Pharmacologist)	In attendance
Dr David Hanlon	National Clinical Advisor and Group Lead Primary Care (General Practitioner)	In attendance
Dr Jerome Coffey	National Director of the National Cancer Control Programme (Medical Consultant)	In attendance
Dr Philip Crowley	National Director for Quality Improvement (Medical Doctor)	By Telephone
Dr Valerie Walshe	Office of the Chief Financial Officer (Economist, PhD)	In attendance
Ms Joan Donegan	Office of Nursing & Midwifery Services (Director of Nursing)	Apologies received
Dr Roy Browne	Mental Health Division (Consultant Psychiatrist)	In attendance
n/a	Social Care Division	Position vacant
Dr Kevin Kelleher	Health and Wellbeing Division (Assistant National Director – Public Health Physician)	In attendance
Ms Angela Fitzgerald	Acute Services Division (Assistant National Director)	Apologies received

In attendance (non-voting):

Secretariat:
Mr Shaun Flanagan (CPU PCRS)
Ms Jennifer McCartan (CPU PCRS)
Ms Ellen McGrath (CPU PCRS)
Ms Kate Mulvenna (Head of Pharmacy Function, PCRS)

HSE Drugs Group – December Minutes

Meeting 2018.11: Tuesday 11th December 2018, 14.00
Board Room, Unit 4A, The Dargan Building, Heuston South Quarter, Military Road, Kilmainham, D8

Dr David Hanlon was agreed as Chair in the absence of Dr Áine Carroll.

1. Draft Minutes for Consideration
    i. The minutes of the meeting of the 9th and 23rd October 2018 were agreed.
    ii. Minutes for 13th November had not been circulated in advance and so were not available for approval.

2. Declaration of Interests / Nil Interest

No conflicts of interest arose. One member raised a potential personal conflict they may have. The members agreed that the matter declared did not represent a conflict.

3. Matters arising / Update on Medicines considered at previous meetings

CPU provided the members with an update in relation to items previously considered. CPU confirmed that the positive recommendations with SLT currently would amount to an estimated budget impact of €130m+ over 5 years.

4. Updates:
    i. Rare Diseases TRC:

The Drugs Group discussed documentation circulated (the RDTRC statement on Nusinersen and a draft clinical guideline). The Group noted that the Rare Diseases TRC PACE statement recommendations for Nusinersen were significantly different to those previously arrived at by the Drugs Group. The Group agreed that it would be important that it carry out a full review of the medicine at its next meeting (January 2019) and that review should include a full and thorough consideration of the Rare Diseases TRC PACE review and the final clinical guideline.

Given the guidelines were in draft and the already large agenda of the December Drugs Group Meeting (5 medicines for review) the group agreed it would not be appropriate to seek to make a recommendation on such a profound issue without having the final guidelines and without having sufficient time to fully consider the issues arising from same.

The Group agreed that what it found particularly helpful (in addition to a PACE review) in previous deliberations which involved a RD TRC review was the provision of robust clinical / reimbursement guidelines with very clear start-stop criteria which were not open to misinterpretation. The group requested that this point be flagged to the RD TRC members as they complete their review of the guidelines.

5. Medicines for Consideration
    i. 18027 Avelumab for Merkel Cell Carcinoma

The Drugs Group by majority supported reimbursement of Avelumab for previously treated Merkel Cell Carcinoma on the basis of a commercially confidential offer received. Due to the uncertainty in the clinical data available to date and resulting uncertainty in the cost-effectiveness the Group asked that CPU request additional information / additional readouts from Merck Serono in relation to 1st line use and when that information is available that the medicine return to Drugs Group.

ii. 18029 Mercaptamine for Cystinosis

The Drugs Group had significant concerns in relation to the proposed pricing and the opportunity costs for other services which could arise. However the Group also noted patient / family testimonies detailing the challenges around the existing formulation and their hopes that a twice daily formulation could improve quality of life for both patients and carers / families.

The Drugs Group agreed it could not support reimbursement at the current commercial offering. However, the Drugs Group agreed that it would recommend reimbursement of Procysbi to the HSE Senior Leadership team **IF** Chiesi were in a position to concede certain additional terms which the Group directed CPU to communicate to the company.

The Group considered this position would still represent a considerable premium over current available alternatives but it noted the proposed advantages conferred by a modified release preparation for the small number of patients affected with this rare disease.

iii. 18030 Nivolumab for Urothelial Cancer

The Drugs Group struggled with the single arm Phase 2 evidence which resulted in significant uncertainty around both the clinical effectiveness and the cost effectiveness evidence.

The Group agreed that the potential budget impact could be somewhat higher than the budget impacts associated with previous decisions around Immunotherapies where the Group had accepted Phase 2 trial evidence.

Additional concerns arose in relation to the complexity of the [redacted] agreement. Whilst the Group had agreed to the [redacted] in the context of 2nd line NSCLC to break a then long running impasse it was concerned that national collection of additional data points not automatically included in reimbursement systems was not a preferred route.

The Group asked CPU to re-engage with BMS to seek an update in relation to any additional data readouts (or additional clinical evidence that might be available in the near future).

The Group also asked that CPU / NCCP meet with BMS to see if there were ways of simplifying the [redacted] data collection proposed for this application. The Group unanimously decided it could not make a recommendation on the basis of the information available.

iv. 18013 Osimertinib for T790M mutation positive non-small cell lung cancer

The Drugs Group noted the principal efficacy endpoints from the phase 3 controlled AURA3 study including the 5.7 months median improvement in investigator assessed progression free survival and the objective response rate (including the CNS response).

The Group noted that overall survival data is not yet mature but a high level of treatment-switching (67.1% crossover at 1st interim analysis) from platinum doublet chemotherapy (PDC) to Osimertinib after progression is expected to confound the interpretation of the final results.

It noted the AstraZeneca argument / claim that compared to historical cohorts (and with statistical adjustments for the impact of crossover) Osimertinib would offer overall survival benefits. The Group noted that the overall safety profile for Osimertinib appears better than that reported for chemotherapy.

The Group noted the price proposed, the poor evidence in relation to cost effectiveness and the budget impact. The Drugs Group unanimously did NOT support reimbursement of Osimertinib

(Tagrisso®) for the treatment of adult patients with locally advanced or metastatic epidermal growth factor receptor (EGFR) T790M mutation positive NSCLC.

Key drivers of the recommendation were the high budget impact in the context of the weak evidence in relation to cost effectiveness. The Drugs Group did not consider that there was a substantial difference between the current commercial offering and the previous commercial offering.

v. 18031 Dinutuximab beta for Neuroblastoma

The Drugs Group considered that the review of Dinutuximab beta was very challenging given the heavy reliance on historical cohort comparators. The Group recognised that the treatment of neuroblastoma involved complicated & difficult to tolerate regimens and that it would wish to support reimbursement of Dinutuximab beta if possible.

The Group noted the clinical evidence submitted, including the views from a clinical expert. The Group noted the clear concerns of the NCPE in relation to the economic models submitted (even with NCPE preferred assumptions) but decided that it would accept the economic models (as adapted) to assist in decision making.

The Group agreed it could not ignore that the funding of Dinutuximab at the price proposed would result in opportunity costs for other services and other patients. The Group unanimously agreed that it would support funding provided that the Cost/QALY in high risk neuroblastoma did not exceed [redacted] under the NCPE preferred assumptions and provided the Cost/QALY in relapsed refractory neuroblastoma did not exceed €45,000/QALY under the NCPE preferred assumptions. The Group flagged that €45,000/QALY is accepted as the upper limit of what a cost effective intervention would be and therefore ARGUABLY may represent a reasonable use of resources.

CPU was instructed to revert to the company and seek terms as per above. The Drugs Group unanimously agreed that a positive recommendation would be in place at those terms.

6. AOB: no AOB arose

7. Proposed Dates for 2019: the dates for 2019 for the new Group had been circulated.

Appendix 1: Members Present

Member	Title	11th Dec2018
Prof. Áine Carroll	Chair, Medical Consultant	Apologies received
Ms Anne Marie Hoey	Primary Care Reimbursement Service (Assistant National Director)	In attendance
Prof. Michael Barry	Medicines Management Programme / National Centre for Pharmacoeconomics (Clinical Director - Consultant Pharmacologist)	In attendance
Dr David Hanlon	National Clinical Advisor and Group Lead Primary Care (General Practitioner)	In attendance (Chair for meet))
Dr Jerome Coffey	National Director of the National Cancer Control Programme (Medical Consultant)	In attendance
Dr Philip Crowley	National Director for Quality Improvement (Medical Doctor)	Apologies received
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
n/a	Social Care Division	Position vacant
Dr Kevin Kelleher	Health and Wellbeing Division (Assistant National Director – Public Health Physician)	In attendance
Ms Angela Fitzgerald	Acute Services Division (Assistant National Director)	In attendance

In attendance (non-voting):

Secretariat:
Mr Shaun Flanagan (CPU PCRS)
Ms Jennifer McCartan (CPU PCRS)
Ms Ellen McGrath (CPU PCRS)
Ms Kate Mulvenna (Head of Pharmacy Function, PCRS)