Drugs Group Minutes: Meeting of 10th April 2018 2pm
Venue: Boardroom, Dr Steeven's Hospital

1. Minutes of March 2018

Minutes of the March meeting were not available for consideration. It was agreed these would be reviewed at the next meeting.

2. Matters arising

CPU provided an update in relation to a number of medicines previously considered

- Palbociclib (Breast Cancer)
- Nusinersen (Spinal Muscular Atrophy)
- Ixazomib (Multiple Myeloma)
- Pertuzumab ((Neo-adjuvant Breast Cancer)
- Mepolizumab (Severe Asthma)
- Reslizumab (Severe Asthma)
- Nivolumab (Head & Neck SCC)
- Nivolumab (2nd Line NSCLC)
- Elosulfase alfa (MPS IVA)

3. Medicines for Consideration

All members confirmed they did not have any potential conflicts for declaration.

a. 18007 Hydrocortisone MR for Addisons Diseases

The Drugs Group discussed the evidence submitted, the commercial offering and the representations received from clinicians. Security and continuity of supply and the pricing history of the immediate release formulation was also discussed. The differences between immediate release, modified release hydrocortisone and physiological profiles were noted.

The Group agreed that notwithstanding representations from Consultant Endocrinologists and the IES it could not recommend in favour of reimbursement. Evidence in relation to any potential benefits over therapies currently available was weak and insufficient to support additional funding required. This recommendation was unanimous. The Group understood that the offer from Shire was its full and final offering.

The negative recommendation would be progressed to National Leadership.

b. 17016 Obeticholic acid for Primary Biliary Cholangitis/Cirrhosis (PBC)

The Drugs Group reviewed the detailed information in relation to Obeticholic acid and the revised commercial offerings. The Drugs Group discussed the potential for the medicine to reduce long term liver complications. It noted that long term studies were ongoing to provide an answer to this question.

Following a discussion, the Drugs Group voted by majority against recommending in favour of reimbursement on the basis of the current commercial offering. 3 members of the group voted in favour of reimbursement.

The Drugs Group also noted that it had discussed the medicine in detail in February 2018. At that meeting, the Group had come to the conclusion that it would most likely be minded to support reimbursement if:

- There was a significantly enhanced commercial offering
- Reimbursement was conditional on the application of robust Start-Stop and Monitoring Criteria

The Group (in February 2018) had discussed what a significantly enhanced offering would involve (i.e. [redacted]) and CPU had been instructed to re-engage with Intercept to seek those commercial terms. Intercept had been unable to meet these terms to date.

The Drugs Group agreed (by majority) that if the specific conditions previously set out were met it would support reimbursement. 2 members of the Group did not support reimbursement.

4. AOB / Members Time

i. The Chair outlined the process to be followed in the event of individual lobbying of Drugs Group members i.e. all such contacts to be referred to the Secretariat (CPU).

ii. The Chair outlined that a number of freedom of information requests were being received in relation to the Drugs Group and these were being dealt with in compliance with the relevant legislation. The Drugs Group noted same.

iii. The Chair confirmed that a Drugs Group paper was being drafted at National Director level in the HSE for consideration by the HSE Leadership and that the membership would be kept updated in relation to same. The members requested that they be given an opportunity to input on the final draft before it was considered at Leadership.

iv. The members noted that a draft bill proposing amendments in relation to Orphan medicines had been circulated within the Oireachtas.

v. CPU was asked to produce a summary in relation to UK processes for a future meeting.

Appendix 1: Members Present

Dr Áine Carroll	Chair, National Director of Clinical Strategy and Programmes (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 O'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)	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 (Item 3(b) on)
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, (PCRS)

Observer: Dr Róisín Adams, Chief Pharmacist, Acute Hospital Division

Drugs Group Minutes: Meeting of 8th May 2018 2pm
Venue: Boardroom, Dr Steeven's Hospital

1. **Minutes of Previous Meetings**
    a. Minutes of March 2018 were reviewed and the members suggested some corrections and clarifications
    b. Minutes of April 2018 were approved

2. **Declaration of Interests / Nil Interests**: All members confirmed they did not have any potential conflicts for declaration. SF (CPU Secretariat) declared a potential conflict of interest in relation to one AOB item. It was agreed SF would remove himself from the meeting for consideration of that item.

3. **Matters arising**: No issues arose which were not already for discussion on the agenda

4. **Medicines for Consideration**

    a. 17003 Carfilzomib for Multiple Myeloma (Resubmission)

The combination of Carfilzomib plus Lenalidomide plus Dexamethasone (CAR+LEN+DEX) had been reviewed on 5 occasions by the Drugs Group. The Group had struggled with the absence of direct comparator data for CAR+LEN+DEX vs Bortezomib (BOR)+LEN+DEX and the uncertainty this created in the cost-effectiveness analysis. The CAR+LEN+DEX combination was expected to be primarily used in fitter patients currently likely to receive BOR+LEN+DEX.

Following a Drugs Group negative recommendation (Feb 2018) which had been progressed to Leadership, Amgen asked that Leadership considerations be stalled. Amgen then provided a further substantially revised commercial offering in additional discussions with CPU and also re-engaged with the NCPE to seek to reduce the level of uncertainty in the economic modelling.

The Drugs Group reviewed the revised offering. It was agreed that cost effectiveness had improved (and the confidence intervals around the estimates had narrowed considerably). The 5 year budget impact was substantially reduced over previous offers.

The Drugs Group by majority decided that the revised offer enabled it to support reimbursement of Carfilzomib (CAR) (Kyprolis®) in combination with Lenalidomide (LEN) and Dexamethasone (DEX) for the treatment of adult patients with multiple myeloma who have received at least one prior therapy. There was one vote against reimbursement.

Following the vote, the members discussed the multiple reviews of Carfilzomib. The members directed that CPU communicate to Amgen the Drugs Group frustration in relation to the initial pricing position.

The Drugs Group asked that CPU make clear the Drugs Group position that where a company (applicant) is submitting for pricing and reimbursement the onus and responsibility remains on the applicant company (who can stand to gain millions of euros in public funds) to put forward a robust dossier and offering which clearly demonstrates that the medication represents both an enhancement over realistic comparators and **reasonable** value for money. If the final offer had been submitted earlier in the process it could have significantly shortened the review process. Whilst the Drugs Group understood the challenges in relation to comparators in this specific case, it still had been the case that the Drugs Group has been expected to make a multi-million

euro investment recommendation in the absence of direct comparator evidence against the most likely comparators and for most of the deliberative process at a price level which bore no relation to the final offering proposed.

b. 18002 Nusinersen for Spinal Muscular Atrophy (Resubmission)

The HSE Drugs Group had previously considered Nusinersen at its March 2018 meeting. An improved commercial offering had been tabled by Biogen following the March 2018 meeting. Nusinersen has market authorisation for the treatment of 5q Spinal Muscular Atrophy (SMA). Spinal Muscular Atrophy is a heterogeneous genetic neurodegenerative disease. There are 5 clinical subtypes (O, I, II, III, IV) classified according to age of symptom onset and the patients best status in terms of motor milestones achieved prior to degeneration.

The Drugs Group agreed that there was a significant unmet need for new treatments for SMA. The Drugs Group considered that there was robust evidence that Nusinersen improved motor milestone responses and that event-free survival was significantly prolonged over the time period of the Phase 3 ENDEAR trial in Type I SMA. Whilst the reported responses were notable and clinically important in the context of the disease, at the time of the final analysis of ENDEAR 39% (31/80) of patients in the Nusinersen arm unfortunately still died or required permanent ventilation.

In reviewing the price proposed, the Drugs Group believed given the unmet need that it was reasonable to consider the widest possible perspective in terms of cost effectiveness (i.e. a societal perspective which included additional patient and caregiver benefits). The Drugs Group believed that it would be in a positon to recommend Nusinersen for Type I SMA if cost effectiveness could be improved to satisfy / approach a cost effectiveness threshold of €45,000 per QALY based on the wider societal perspective model submitted by the company.

The Drugs Group also considered the evidence submitted in relation to Type II or Type III (later-onset) SMA. The clinical evidence submitted in relation to Type II and III SMA was less convincing than that for Type I SMA. In the Phase 3 CHERISH study motor function improvements were demonstrated. The economic evidence submitted was less robust for Type II and III SMA.

On the basis of the evidence submitted to date the Drugs Group was unable to recommend reimbursement of Nusinersen for Type II and III SMA. The Drugs Group noted that some other international countries had sought to prioritise reimbursement towards Type I SMA.

c. 18008 Everolimus for refractory partial-onset seizures associated with tuberous sclerosis complex

The Drugs Group decided unanimously that a full Health Technology Assessment was required to enable it to make a recommendation to HSE Leadership.

d. 18003 Ixazomib for Multiple Myeloma (Resubmission)

The Drugs Group agreed that there was insufficient time remaining to robustly consider the submission from Takeda.

5. **AOB**

a. Duodopa for Parkinsons Disease

The Drugs Group unanimously agreed that the HSE should continue to honour the previous agreement made with Abbvie that resources would be made available to support the reimbursement of [redacted] patients. The onus remained on the company to submit a dossier containing sufficient evidence to robustly demonstrate that reimbursement was a cost effective use of resources. The Drugs Group expected that Abbvie would honour previous commitments made.

b. Teduglutide for Short Bowel Syndrome

The Drugs Group agreed that CPU would engage with Shire in relation to commercials while in parallel the design of a potential reimbursement model could be progressed with Rare Diseases TRC. The Drugs Group did NOT discuss whether it would be in a position to recommend reimbursement and did NOT consider any recommendation in relation to reimbursement.

c. Nivolumab: Update on Fixed Dose Market Authorisation Variation

The Drugs Group was provided with an update in relation to fixed dose Nivolumab and a comparison to prices considered under various HTAs and a price comparison to pembrolizumab. The Group agreed that no issues arose for it to consider.

6. **Members Time**

a. UK Kings Report: Rising Cost of Medicines (VW)

The Group noted the report which provided interesting statistics and commentary on challenges faced by NHS England. MB flagged to members a series of communications in the Value in Health Journal.
Rare Diseases: https://www.valueinhealthjournal.com/article/S1098-3015(18)30282-1/fulltext
Affordability: https://www.valueinhealthjournal.com/issue/S1098-3015(18)X0002-3

b. Leadership Paper on Drugs Group (in draft)

The Drugs Group noted the draft paper. It was agreed that members would provide any feedback by May 15th.

Appendix 1: Members Present

Dr Áine Carroll	Chair, National Director of Clinical Strategy and Programmes (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 O'Hanlon	National Clinical Advisor and Group Lead Primary Care (General Practitioner)	In attendance
Ms Patricia Heckmann For Dr Jerome Coffey	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)	Not 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)	By telephone until 310pm
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)	By telephone
Ms Angela Fitzgerald	Acute Services Division (Assistant National Director)	Apologies received

In attendance (non-voting):

Secretariat:
Mr Shaun Flanagan (CPU PCRS) (left meeting for part of AOB),
Ms Jennifer McCartan (CPU PCRS),
Ms Ellen McGrath (CPU PCRS),
Ms Kate Mulvenna, (PCRS)

Drugs Group Minutes: Meeting of 12th June 2018, 14.00

Venue: Boardroom, Dr Steevens Hospital

1. **Minutes of Previous Meetings**
    a. Minutes of March 2018 were approved (corrections had been provided at May meeting)
    b. Minutes of May 2018 were approved

2. **Declaration of Interests / Nil Interests**: One member declared that they knew a family who had a child with SMA. It was agreed this did not constitute a reason to withdraw from meeting albeit the member abstained from deliberations on Nusinersen. All other members confirmed they did not have any potential conflicts for declaration.

3. **Matters arising**: No issues arose which were not already for discussion on the agenda

4. **Medicines for Consideration**

    a. 18003 Ixazomib for relapsed/refractory multiple myeloma

On the basis of the evidence available, the Group decided unanimously that it would not be in a position to support any premium in the pricing of / commercial terms around Ixazomib over previous medicines considered for similar indications.

    b. 18010 Benralizumab for eosinophilic asthma

The Drugs Group carefully considered the clinical and economic evidence. The Drugs Group noted that a full health technology assessment had been recommended but also that it had considered a number of medicines for similar indications in the recent past.

The Drugs Group unanimously decided it could not support reimbursement on the basis of the offer tabled by AstraZeneca. However the Group decided in the interest of efficiency that it would be prudent to provide clarity on the commercial offering that it would be minded to recommend.

The Drugs Group agreed it could make a positive recommendation on a cost minimisation assessment rationale if AZ were in a position to offer specific terms which it discussed. The Drugs Group authorised CPU to progress such terms directly to Leadership if they were to emerge i.e. such an offer would not require further review by the Drugs Group.

In the absence of such an offer, the Drugs Group recommended that the full health technology assessment should be progressed.

c. 18011 Eliglustat for Gaucher disease

The Drugs Group unanimously supported reimbursement on the basis that this oral medicine was likely to be budget neutral or of lower acquisition cost than intravenous alternatives. It offered convenience for patients albeit that there might be some concerns around non-inferiority. However any such concerns would be for clinicians to discuss with the patients / patients representatives.

d. 18005 Pembrolizumab for cHL

The Drugs Group noted that it had previously at its March 2018 meeting directed CPU to re-engage with MSD to see if it could achieve a solution which would allow it to consider this application in the context of a cost minimisation approach. In addition the Drugs Group had asked the NCCP to complete some additional analysis in relation to the issue of unmet need. The Drugs Group considered the updates in relation to both these actions.

The HSE Drugs Group unanimously recommended in favour of reimbursement of Pembrolizumab (in the absence of a full health technology assessment) for the following RESTRICTED use for which an unmet need was noted: monotherapy for the treatment of adult patients who are transplant-ineligible and have failed brentuximab vedotin.

On the basis of the proposed price, which was not comparable with current available therapies, reimbursement was unanimously NOT recommended for monotherapy for the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma (R/R cHL) who have failed autologous stem cell transplant (auto-SCT) and brentuximab vedotin (BV).

e. 18012 Pembrolizumab for 2L NSCLC

The Drugs Group carefully reviewed the clinical and economic evidence in relation to this medicine. The Drugs Group was unable to support reimbursement on the basis of the current commercial offering.

The Drugs Group unanimously agreed it could make a positive recommendation if MSD were in a position to offer additional terms and the Drugs Group provided direction to CPU on an offer level that it (the Drugs Group) would support.

The Drugs Group authorised CPU to progress such terms directly to Leadership if they were to emerge i.e. they would not require further review by the Drugs Group.

f. 18013 Osimertinib for NSCLC

There was insufficient time available to discuss this application.

5. Feedback and Discussion on Previous Recommendations

a. 17017 Nivolumab for NSCLC - ND request for review (Slides 36 & 37, 17017c)

At the request of the HSE Leadership team, the Drugs Group examined the revised offering from BMS at its June 2018 meeting. The Drugs Group was unable to support reimbursement on the basis of the revised offer.

However, the Drugs Group agreed that given the efforts on both sides to find a resolution it should examine and provide clarity on a commercial arrangements it could support.

The Drugs Group unanimously agreed it could make a positive recommendation on the basis of the current offer if BMS were in a position to offer an additional term and the Drugs Group gave CPU clear direction on an offer level that it (the Drugs Group) would support.

The Drugs Group authorised CPU to progress such terms directly to Leadership if they were to emerge i.e. they would not require further review by the Drugs Group.

b. 18002 Nusinersen for SMA – direction on commercial proposal (Slides 36 & 37)

The Drugs Group considered Biogen's revised commercial proposal. The Drugs Group decided that the offer did not address its concerns of May 2018.

The Drugs Group reiterated its belief that it would be in a positon to recommend Nusinersen for Type I SMA if cost effectiveness could be improved to satisfy / approach a cost effectiveness threshold of €45,000 per QALY based on the wider societal perspective model submitted by the company i.e. based on the most optimistic estimates of cost effectiveness.

The Drugs Group reiterated that on the basis of the evidence submitted to date the Drugs Group was unable to recommend reimbursement of Nusinersen for Type II and Type III SMA. 1 member abstained so as to avoid any potential conflict of interest. 1 other member abstained.

c. 17016 Obeticholic acid for Primary Biliary Cholangitis/Cirrhosis (PBC) –

There was insufficient time available to discuss this application.

d. Eltrombopag for cITP

There was insufficient time available to discuss this application.

6. AOB / Members Time

a. Oireachtas Report on Orphan Medicines

The report had been provided to members in advance. The members did not discuss the report.

Appendix 1: Members Present

Dr Áine Carroll	Chair, National Director of Clinical Strategy and Programmes (Medical Consultant)	In attendance
Ms Kate Mulvenna For Ms Anne Marie Hoey	Primary Care Reimbursement Service, Head of Pharmacy Function, For 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)	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)	Apologies Received
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),

Observer: Dr Róisín Adams, Chief Pharmacist, Acute Hospital Division