AWTTC
All Wales Therapeutics & Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

Interim Pathways Commissioning Group (IPCG)

Minutes of the meeting held Monday 25 November 2019 in the MDT Room, Routledge Academic Centre, University Hospital Llandough, Cardiff CF64 2XX

Members in attendance:
Andrew Champion, Assistant Director, Evidence Evaluation, IPFR representative WHSSC, IPCG deputy Chair
Alan Clatworthy, Clinical Effectiveness and Formulary Pharmacist, Swansea Bay
Ian Campbell, Hospital Consultant CAV, NMG representative
Richard Hain, Consultant in Paediatric Palliative Care, Cardiff and Vale
Jonathan Simms, Clinical Director of Pharmacy, Aneurin Bevan
Jayne Price, Deputy Head of Pharmacy, Powys
Malcolm Latham, Community Health Council
Brian Hawkins, Chief Pharmacist, Medicines Management, Cwm Taf Morgannwg
Rick Greville, Director of ABPI Wales
William King, Consultant in Public Health, Powys
Hywel Pullen, Assistant Director of Finance, WHSSC

Via videoconference:
Will Oliver, Assistant Director of Therapies and Health Science, Hywel Dda
Teena Grenier, Medicines Governance Lead, Betsi Cadwaladr

Via teleconference:
Berni Sewell, Health Economist, Swansea University

Observer:
John Watkins, Consultant in Public Health

AWTTC:
Tony Williams, Senior Appraisal Pharmacist, Team Leader
Gail Woodland, Senior Appraisal Pharmacist
Rosie Spears, Senior Appraisal Scientist
Jessica Davis, Senior Appraisal Scientist
Rob Bracchi, Medical Director

Clinical experts:
Dr Sinan Eccles, Consultant Respiratory Medicine, Cwm Taf Morgannwg (via videoconference)

List of Abbreviations:

ABPI	Association of the British Pharmaceutical Industry
AWTTC	All Wales Therapeutics & Toxicology Centre
ESR	Evidence Status Report
IPCG	Interim Pathways Commissioning Group
IPFR	Independent Patient Funding Request
NICE	National Institute for Health and Care Excellence
NMG	New Medicines Group
WHSSC	Welsh Health Specialised Services Committee

1. Welcome and Introduction

The Chair opened the meeting and welcomed members.

2. Apologies

James Coulson, Clinical Pharmacologist, Cardiff and Vale
Laurence Gray, Consultant, Cardiff and Vale
Bethan Tranter, Chief Pharmacist, Velindre Trust
Simon Waters, Consultant Oncologist, Velindre Trust

3. Declaration of Interests/Confidentiality

The Chair reminded members that all IPCG proceedings are confidential and should not be disclosed outside of the meeting. Members were reminded that declarations of interest and confidentiality statements are signed by each member on an annual basis. Members were asked to ensure they had signed and returned the confidentiality statements for 2019 to AWTTC. The Chair invited any declarations of interest; there were none.

4. Chair's report

The Chair announced that the Chief Executive Management Team has endorsed the medicines considered at the meetings held on 29 May (virtual meeting) and 24 June:

- rituximab as second- or third-line treatment of fibrotic interstitial lung disease (not idiopathic pulmonary fibrosis) associated with connective tissue disease or idiopathic fibrotic non-specific interstitial pneumonia
- rituximab for the fourth-line or later treatment of refractory myasthenia gravis in adults
- review of denosumab for the treatment of osteoporosis in men at increased risk of fractures
- review of bendamustine in combination with rituximab for the treatment of previously untreated and relapsed indolent lymphomas
- review of bendamustine in combination with rituximab for the treatment of previously untreated and relapsed mantle cell lymphoma therapy
- re-assessment of low dose bevacizumab for the front-line treatment of advanced high risk ovarian cancer
- One Wales advice for docetaxel for treatment of hormone-sensitive prostate cancer to be retired as it is now standard practice and included in NICE Guideline published September 2019.

The Chair announced that the IPCG recommendation for cannabidiol for the treatment of Lennox-Gastaut and Dravet syndromes was endorsed by the Chief Executive Management Team. However, the indication for cannabidiol considered by IPCG was different to the licensed indication which was subsequently issued, therefore the One Wales assessment was terminated. AWTTC contacted the company and requested that they submit new information for re-consideration by One Wales, in line with the licensed indication. In the meantime, the NICE final appraisal determination was published and the advice from One Wales was no longer required.

The recommendation from today's meeting and the review of rituximab for pemphigus and pemphigoid disease which was considered at the virtual September meeting, will be forwarded to the Chief Executive Management Team for their consideration on 17 December 2019.

5. Assessment 1
Mepolizumab (Nucala®▼) for the treatment of chronic eosinophilic pneumonia.

The Chair briefly outlined the sequence of events and set the context of the meeting.

The Chair invited any declarations of interest specific to this assessment; there were none.

Rosie Spears presented the key aspects of the evidence status report.

The Chair introduced the clinical expert, Dr Sinan Eccles. The Chair described the role of the clinical expert as an invited observer of the IPCG meeting to answer questions and input into discussions to enable members to gain a better understanding of the clinical context. The Chair highlighted that clinical experts were nominated by their specialist group or network and should not express personal opinion or promote the use of a medicine.

The Chair invited the clinical expert to give an overview of the disease and medicine being considered. The clinical expert explained that chronic eosinophilic pneumonia (CEP) is not easily diagnosed, it presents with non-specific symptoms such as cough, fever and weight loss and often presents with pneumonia. CEP is often misdiagnosed as asthma and is commonly diagnosed in patients aged 30 to 50 years. Most patients respond well to oral corticosteroids. The problem arises when tapering steroids where some people relapse and the disease becomes chronic. The clinical expert highlighted the lack of evidence around mepolizumab for the treatment of CEP, and noted that it is unlikely that randomised controlled trials will be forthcoming as CEP is often latched onto other conditions. There are case reports and anecdotal evidence showing that mepolizumab is effective for the treatment of CEP; mepolizumab has been shown to be effective in patients with asthma and CEP. The clinical expert noted the high cost of mepolizumab, but added that this medicine would decrease the need for steroids and immunosuppressants and the associated side effects.

The Chair opened general discussion relating to the clinical effectiveness of mepolizumab. Members asked about the treatment pathway, where mepolizumab would be placed and what dose would be used. The clinical expert stated that preferably mepolizumab would be used for patients who relapse when weaning off steroids; currently these patients either remain on high-dose steroids or receive azathioprine or mycophenolate mofetil. The asthma dose has been used in studies, and the clinical expert was not aware of studies using a lower dose or the effectiveness at this dose. Members questioned how often azathioprine and mycophenolate mofetil are not tolerated or not effective. It was noted that a large number of patients (around 45%) do not tolerate azathioprine; mycophenolate mofetil is tolerated a little better. Members asked about other biologic medicines e.g. reslizumab and omalizumab. It was highlighted that mepolizumab has the most literature and it has been around the longest. There are services in Wales to deliver mepolizumab as there are patients already receiving it through asthma services. It is unlikely that other biologics would be needed.

The estimated patient numbers and patient cohort were discussed. The estimated 35 patients in Wales is based on extrapolation, and includes patients with a co-diagnosis of asthma and patients already receiving mepolizumab. Therefore, the patient numbers are likely to be fewer than 35. Members asked about the criteria for stopping treatment. The clinical expert noted that for patients with asthma, and in line with the NICE guidance, treatment would be stopped at 12 months if a response were not achieved. A response to treatment of CEP can be predicted at around four to six months,

particularly if there is a reduction in steroid dose. Gail Woodland highlighted that if mepolizumab was supported for use through One Wales, specific starting and stopping criteria would be developed. Members asked about the administration of mepolizumab. The clinical expert confirmed that mepolizumab is currently given in secondary care; there is a mechanism for it to be given in the community and to be self-administered though this is not yet in place. Members discussed the weak evidence base and asked whether there would be a commitment from clinicians to report outcome data if mepolizumab were to be made available. The clinical expert confirmed that outcome data would be reported.

The Chair invited discussion of any cost-effectiveness issues. Members noted that there were no cost-effectiveness studies and that cost-effectiveness analyses from the NICE technology appraisal of mepolizumab for the treatment of asthma had been provided as a proxy. The health economist questioned whether there is any evidence that the quality of life of patients with eosinophilic asthma can be aligned with patients with CEP and whether the efficacy of mepolizumab is the same in both conditions. It was noted that the relapse is not the same in both conditions; patients with eosinophilic asthma experience an exacerbation whereas patients with CEP usually experience deterioration. Members discussed the high cost of mepolizumab compared with immunosuppressants. The clinical expert highlighted that the toxicities of immunosuppressants are the concern and noted the difficulty in modelling the costs of adverse events and monitoring associated with immunosuppressants. Members noted that the driver of the cost-effectiveness model was a decrease in exacerbation and questioned whether mortality was also a driver. It was highlighted that it would be very difficult to capture death due to CEP. Members asked what proportion of patients would receive lifelong mepolizumab treatment. The clinical expert said that a proportion of patients would have lifelong treatment and others would go through natural attrition. The benefits of treatment would be reviewed at 12 months and a decision made whether to stop treatment. The health economist added that it is difficult to calculate the incremental cost-effectiveness ratio. The Chair invited discussion of any budget impact issues. Members discussed the 50% response rate. It was noted that this figure is uncertain.

The Chair invited discussion on the patient and public perspective. The lay member highlighted that patients would likely prefer to have mepolizumab as opposed to long-term steroids and the associated side effects.

The clinical expert left the meeting and members were invited to vote. The IPCG recommendation for health board Chief Executives was agreed:

Date of advice: Monday 25 November

It is the view of the Interim Pathways Commissioning Group (IPCG) that mepolizumab (Nucala®) should not be supported within NHS Wales for the treatment of chronic eosinophilic pneumonia.

Individual Patient Funding Request (IPFR) consideration remains appropriate for those patients who are likely to obtain significantly more clinical benefit from the intervention than would normally be expected at a reasonable value for money.

This advice will be reviewed after 12 months or earlier if new evidence becomes available.

6. Minutes of the previous meeting

The draft minutes of the June IPCG meeting were checked for accuracy and confirmed. It was confirmed that the minutes of the meeting would be made available on the AWTTC website.

7. Date of next meeting

The Chair confirmed that the next meeting will be on 27 January 2020. The Chair then thanked members for their participation and closed proceedings.