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

Interim Pathways Commissioning Group (IPCG)

Minutes of the meeting held Monday 29 April 2019 in the MDT Room, Academic Centre, University Hospital Llandough, Cardiff CF64 2XX

Members in attendance:
Sharon Hopkins, Deputy Director of Transformation and Informatics, CAV, IPCG Chair
Alan Clatworthy, Clinical Effectiveness and Formulary Pharmacist, Swansea Bay
Ian Campbell, Hospital Consultant CAV, NMG representative
Fiona Woods, Director, WMIC, CAV
Andrew Champion, Assistant Director, Evidence Evaluation, IPFR representative WHSSC
Bethan Tranter, Chief Pharmacist, Velindre Trust
Jonathan Simms, Clinical Director of Pharmacy, Aneurin Bevan
Jayne Price, Deputy Head of Pharmacy, Powys
Malcolm Latham, Community Health Council

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

Via teleconference:
Jo Charles, Research Fellow, Welsh Health Economics Support Service

AWTTC:
Phil Routledge, Clinical Director
Karen Samuels, Head of Health Technology Assessment, Medicines Management and Programme Director
Gail Woodland, Senior Appraisal Pharmacist
Rosie Spears, Senior Appraisal Scientist
Jessica Davis, Senior Appraisal Scientist
Bridget-Ann Kenny, Medical Writer
Rob Bracchi, Medical Director

Clinical experts:
Dr Ben Hope-Gill, Respiratory Consultant, CAV
Dr Marguerite Hill, Consultant Neurologist, Swansea Bay (via teleconference)

List of Abbreviations:

ABPI	Association of the British Pharmaceutical Industry
AWPAG	All Wales Prescribing Advisory Group
AWTTC	All Wales Therapeutics & Toxicology Centre
CAV	Cardiff and Vale
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
WHESS	Welsh Health Economic Support Service
WHSSC	Welsh Health Specialised Services Committee
WMIC	Welsh Medicines Information Centre

1. Welcome and Introduction
The Chair opened the meeting and welcomed members.

2. Apologies
James Coulson, Clinical Pharmacologist, CAV
Rick Greville, Director of ABPI Wales
Joe Ferris, Operations Manager, ABPI Wales
Brian Hawkins, Chief Pharmacist, Medicines Management, Cwm Taf Morgannwg
Stuart Bourne, Deputy Director Public Health, Powys
Stuart Davies, Director of Finance, WHSSC

3. Minutes of the previous meeting
The draft minutes of the January 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. The Chair informed members that the recommendations from the January IPCG meeting and the virtual IPCG meeting in February had been endorsed by the Chief Executive Team.

4. 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.

5. Assessment 1
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.

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 Ben Hope-Gill. 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 opened general discussion relating to the clinical effectiveness of rituximab. Members questioned whether mycophenolate is currently used in practice. The clinical expert confirmed that mycophenolate is commonly used first-line in patients who are younger and fitter, whereas azathioprine is given to frailer and older patients. The clinical expert highlighted that these patients have progressive disease which is not curable. Due to comorbidities, these patients are not eligible for lung transplant. The tolerability of rituximab is much greater than cyclophosphamide. Given that the disease is variable, conducting large clinical trials is difficult. Members asked what outcome data would be measured. The clinical expert confirmed that in Cardiff and Vale these

would be mortality and lung function, measured by change in FVC, which is also a surrogate marker of mortality. The clinical expert highlighted that an all Wales web-based audit tool is being piloted to track outcomes and is due to be rolled out in 12-24 months. Members questioned the length of rituximab treatment. The clinical expert noted that treatment is variable. Treatment would be started when the FVC decreases by more than 10% in 12 months. Interstitial lung disease is not as aggressive as idiopathic pulmonary fibrosis. If patients experienced a decrease in FVC while receiving rituximab, members asked whether rituximab treatment would be increased to six monthly rather than 12 monthly. The clinical expert said that he would try six monthly doses, otherwise palliative care. Occasionally, an increase in FVC has been seen with rituximab treatment, thus deferring palliative care. Members asked how many people have interstitial lung disease associated with antisynthetase syndrome. The clinical expert confirmed that this is rare, and would likely be classified as mixed connective tissue disease.

The Chair invited discussion of any cost-effectiveness issues. Members noted that there were no cost-effectiveness studies.

The Chair invited discussion of any budget impact issues. Members questioned whether the 1 g rituximab regimen has demonstrated an increase in FVC in clinical trials. The clinical expert noted that due to the rarity of the disease, clinical trials have not been sufficiently powered to establish the most effective dosing regimen. The 1 g rituximab regimen has been adopted. Members asked whether a rituximab biosimilar would be used in practice. The clinical expert noted that there would be no reason why a biosimilar would not be used. Gail Woodland highlighted that if rituximab was supported for use through One Wales Interim Commissioning, starting and stopping criteria would be developed which could specify which product to be used.

The Chair invited discussion on the patient and public perspective. Members asked whether there are any health-related quality of life data available. The clinical expert was not aware of any data. From experience, rituximab is tolerated well compared with intravenous cyclophosphamide.

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 29 April

Using the agreed starting and stopping criteria, rituximab can be made available within NHS Wales for the 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.

The rituximab product with the lowest acquisition cost should be chosen for newly initiated patients.

The risks and benefits of the off-label use of rituximab for this indication should be clearly stated and discussed with the patient to allow informed consent.

Providers should consult the General Medical Council Guidelines on prescribing unlicensed medicines before any off-label medicines are prescribed.

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

6. Assessment 2

Rituximab for the fourth-line or later treatment of refractory myasthenia gravis in adults.

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

Gail Woodland presented the key aspects of the evidence status report.

The Chair introduced the clinical expert, Dr Marguerite Hill. 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 provide the committee with an overview of the clinical context. The clinical expert noted that there are two groups of patients with myasthenia gravis that would benefit from rituximab treatment:

1. The first group are patients who are very sick and do not have time to wait for mycophenolate or azathioprine to work. In these patients, emergency rescue treatment with rituximab, which works very quickly, would delay treatment with IVIg or plasma exchange and keep patients out of intensive care.
2. The second group are patients with myasthenia gravis that has not responded to other immunosuppressant medicines or who cannot tolerate these medicines.

Patients tolerate current medicines very well. Therefore, the number of patients likely to require rituximab treatment is very low. The appropriateness of cyclophosphamide as a comparator was discussed. It was noted that AWTTC-sought clinical expert opinion varied but that some experts considered cyclophosphamide to be an appropriate comparator.

The Chair opened general discussion in relation to clinical effectiveness. Members sought clarification on the dose of rituximab, and whether the lowest acquisition cost product would be used. The clinical expert highlighted that it is difficult to state a dose because no such trials have been conducted. The clinical expert agreed that the Schedule A regimen is mostly used. There would be no reason why a biosimilar could not be used. Members questioned whether muscle specific kinase receptor positive disease is treated different to acetylcholine receptor positive disease. The clinical expert highlighted that muscle specific kinase receptor positive disease is more responsive to rituximab and that there are biological reasons why rituximab works better for this receptor type. Members asked whether eculizumab is used. The clinical expert had no experience of using this medicine. The cost of treatment was noted. Members asked whether NHS England's stop criteria are appropriate. The clinical expert confirmed that it would be reasonable to apply these criteria, and added that it would be obvious in a couple of weeks whether rituximab treatment is working.

The Chair invited discussion on any cost-effectiveness or budget impact issues. There were no additional issues raised.

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

Date of advice: Monday 29 April 2019

Using the agreed starting and stopping criteria, rituximab can be made available within NHS Wales for the fourth-line or later treatment of refractory myasthenia gravis in adults.

The rituximab product with the lowest acquisition cost should be chosen for newly initiated patients.

The risks and benefits of the off-label use of rituximab for this indication should be clearly stated and discussed with the patient to allow informed consent.

Providers should consult the General Medical Council Guidelines on prescribing unlicensed medicines before any off-label medicines are prescribed.

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

7. Assessment 3

Denosumab for the treatment of osteoporosis in men at increased risk of fractures.

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

Jessica Davis presented the key aspects of the review report.

The Chair opened general discussion on the review. Members noted that NICE guidance is expected in September 2019 and that there was no new evidence to warrant a change to the One Wales decision. Members were disappointed with the lack of outcome data.

The IPCG recommendation for health board Chief Executrices was agreed:

Date of advice: Monday 29 April 2019

Denosumab can continue to be made available within NHS Wales for the treatment of osteoporosis in men at increased risk of fractures. Denosumab should only be made available for men who fulfil the agreed criteria for treatment.

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

Advice is interim to subsequent Health Technology Assessment advice from AWMSG or NICE becoming available.

8. Date of next meeting

The Chair confirmed that the next meeting on 29 May 2019 would be a virtual consultation for two reviews.

The Chair then thanked members for their participation and closed proceedings.