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

Interim Pathways Commissioning Group (IPCG)

Minutes of the virtual (Zoom) meeting held Monday 18 May 2020

Members in attendance:
John Watkins, Consultant in Public Health, IPCG Chair
Andrew Champion, Assistant Director, Evidence Evaluation, IPFR representative WHSSC
Alan Clatworthy, Clinical Effectiveness and Formulary Pharmacist, Swansea Bay
Richard Hain, Consultant in Paediatric Palliative Care, Cardiff and Vale
Jonathan Simms, Clinical Director of Pharmacy, Aneurin Bevan
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
Will Oliver, Assistant Director of Therapies and Health Science, Hywel Dda
Teena Grenier, Medicines Governance Lead, Betsi Cadwaladr
Berni Sewell, Health Economist, Swansea University

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
Bridget-Ann Kenny, Medical Writer
Katherine Chaplin, Medical Writer
Laura Phillips, Admin Supervisor

Clinical experts:
Dr Eve Gallop-Evans, Consultant Clinical Oncologist and Clinical Director, Velindre Cancer Centre

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
Bethan Tranter, Chief Pharmacist, Velindre Trust
Ian Campbell, Hospital Consultant CAV, NMG representative

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. 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 30 September (virtual) and 25 November 2019:

- mepolizumab for the treatment of chronic eosinophilic pneumonia
- review of rituximab for the second-line treatment of pemphigus (excluding pemphigus vulgaris) and fourth-line treatment of pemphigoid disease.

Chief Executive Management Team endorsement is pending for the January 2020 review of adalimumab for treatment of paediatric patients with severe refractory non-infectious intermediate, posterior and pan-uveitis.

The Chair announced that in April, in response to the COVID-19 crises, AWTTC conducted a rapid assessment for the use of abiraterone (ZYTIGA®), apalutamide (Erleada®) and enzalutamide (Xtandi®) for the treatment of high-risk locally advanced and metastatic, hormone-sensitive prostate cancer during the COVID-19 pandemic. A Chair's action decision was made and the decision will be reviewed after 3 months.

The recommendation from today's meeting will be forwarded to the Chief Executive Management Team for their consideration on 23 June 2020.

5. Assessment 1

Azacitidine for the treatment of progressive angioimmunoblastic T-cell lymphoma (AITL).

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 Eve Gallop-Evans. 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 defined the population being considered: elderly, frail patients who are chemo-refractory and not fit enough for high dose chemotherapy. These tumours behave as high-grade tumours, although they are classified as low-grade. The clinical expert highlighted the unmet clinical need for these patients. It was noted that there are activating mutations and markers that can be screened for to confirm diagnosis. The clinical expert highlighted their limited experience of using

azacitidine for the treatment of AITL. It was noted that the ORACLE (oral azacitidine) clinical trial, with four centres in England, is recruiting seven patients in the UK.

The Chair opened general discussion relating to the clinical effectiveness of azacitidine. Members requested confirmation on patient population, and that these patients were not suitable for a transplant and the only treatment for survival would be azacitidine. The clinical expert stated that these patients are chemo-refractory and azacitidine controls the disabling systemic symptoms and allows the steroid dose to be reduced. Patients would receive two cycles of treatment and then response would be assessed. Treatment would be stopped if there was no clinical benefit or toxicity. Members questioned the adverse event profile. The clinical expert stated that they have limited experience with this medicine for the treatment of AITL, and most of the literature on safety has been extrapolated from myeloid diseases.

Members asked whether there is a compassionate use program available. The clinical expert and AWTTC were not aware of a compassionate use program in the UK. Members questioned the average age range of patients with AITL. The clinical expert noted that most patients are above 70 years old, with an average age of around mid-70s. It was noted that for younger, fitter patients who relapse after transplant, subsequent treatment is palliative. Members asked about brentuximab for the treatment of CD30+ disease which is due to be reviewed by NICE. The clinical expert highlighted that CD30 is not a diagnostic for AITL or a characteristic phenotype for AITL. Members discussed quality of life. The clinical expert noted that patients experience disabling fatigue, drenching sweats and itching skin rash. The clinical expert provided anecdotal information on the benefits of this medicine in terms of efficacy and quality of life. The clinical expert noted that patients have to attend the day unit every day for 7 days for treatment, every four weeks. During COVID-19, treatment is 6-weekly, rather than 4-weekly.

The Chair invited discussion of any cost-effectiveness issues. The health economist highlighted that there is no cost-effectiveness evidence. It was noted that azacitidine is expensive and that there are a lot of uncertainties; in one study a patient received more than 60 cycles of treatment. The clinical expert noted that at the point of relapse, when azacitidine treatment would be considered, these patients have a poor prognosis with an expected life expectancy of 6-12 months (which equates to 6-12 cycles of treatment). There was a discussion around end of life treatments and rare diseases. Members noted that azacitidine is off-patent and a generic subcutaneous preparation is available, therefore the price may reduce.

The Chair invited discussion on the budget impact. The health economist noted that the budget impact is likely to be higher than that estimated in the ESR if patients were to receive more than six cycles of treatment. Members asked whether gemcitabine could be used for these patients, and is therefore a suitable comparator. The clinical expert confirmed that gemcitabine could be used. Rosie Spears highlighted that during consultation with clinical experts, bendamustine was noted as the most appropriate comparator.

The Chair invited discussion on the patient and public perspective. No submissions had been received from patient organisations.

The Chair invited discussion on the wider societal and health and social care issues. Members asked whether patients in Wales would be considered for the ORACLE trial. The clinical expert confirmed that clinical trials would always be considered first.

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 18 May

Using the agreed starting and stopping criteria, azacitidine can be made available within NHS Wales for the treatment of progressive angioimmunoblastic T-cell lymphoma.

The risks and benefits of the off-label use of azacitidine 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. Minutes of the previous meeting

The draft minutes of the November 2019 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. IPCG membership

Gail Woodland informed members who have been on the committee since its inception, that their membership is due for review (4 years). Members will be contacted in due course.

8. **Next meeting**

The Chair confirmed that the next meeting will be on 29 June 2020. The Chair then thanked members for their participation and closed proceedings.