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

Interim Pathways Commissioning Group (IPCG)

Minutes of the meeting held Monday 24 June 2019 in the MDT Room, Academic Centre, University Hospital Llandough, Cardiff CF64 2XX

Members in attendance:
Alan Clatworthy, Clinical Effectiveness and Formulary Pharmacist, Swansea Bay, IPCG Interim Chair
Ian Campbell, Hospital Consultant CAV, NMG representative
Rick Greville, Director of ABPI Wales
Brian Hawkins, Chief Pharmacist, Medicines Management, Cwm Taf Morgannwg
Malcolm Latham, Community Health Council
Bethan Tranter, Chief Pharmacist, Velindre Trust
Jonathan Simms, Clinical Director of Pharmacy, Aneurin Bevan
Fiona Woods, Director, WMIC, CAV

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

Via teleconference:
William King, Consultant in Public Health, Powys
Bernadette Sewell, Research Fellow, Welsh Health Economics Support Service

AWTTC:
Rob Bracchi, Medical 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
Lucy Lewis, Intern

Clinical experts:
Dr Louise Hannah, Oncology Consultant, Velindre Trust
Dr Frances Gibbon, Consultant Neurologist, CAV

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
Sharon Hopkins, CEO, CTMUHB, IPCG chair
James Coulson, Clinical Pharmacologist, CAV
Stuart Bourne, Deputy Director Public Health, Powys
Stuart Davies, Director of Finance, WHSSC
Andrew Champion, Assistant Director, Evidence Evaluation, IPFR representative WHSSC, IPCG deputy chair

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. Re-assessment
Bevacizumab (Avastin®) at a dose of 7.5 mg/kg in combination with carboplatin and paclitaxel for the front-line treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer.

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.

A statement from the patient organisation Ovacome was provided to the group which provided six patient experiences of treatment with bevacizumab for this indication.

Jessica Davis presented the key aspects of the evidence status report.

The Chair introduced the clinical expert, Dr Louise Hannah. 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 clinical expert confirmed with the group that the group statement from the oncology clinicians had been sent to the IPCG members and that the letter sums up the collective view of the Wales Cancer Network. The Chair opened general discussion relating to the clinical effectiveness of bevacizumab.

The clinical expert expressed the view that the ICON7 clinical trial demonstrated the efficacy of bevacizumab in delaying progression free survival, in particular in the high risk subgroup in which no decrement of quality of life was reported. The expert stated

that in practice, patient experience was in line with those expressed in the statement provided by Ovacome.

Members requested confirmation of the patient group under consideration, the clinical expert explained that the high-risk sub-group as pre-defined in the ICON7 study are identified as most likely to benefit from treatment with bevacizumab as disease which cannot be optimally de-bulked leaves residual disease, the mode of action is such that it reduces formation of blood vessels to remaining tumour. This patient group is the same as that covered by the Cancer Drugs Fund.

Members queried the number of cycles that a patient would receive, noting that several of the patients providing statements in the Ovacome summary had received more than 18 cycles of bevacizumab. The clinical expert stated that most patients in Wales are currently privately funded, however, would expect that patients receive no more than 18 cycles in line with the trial data.

The Chair invited discussion of any cost-effectiveness issues. AWTTC confirmed that the cost-effectiveness calculations provided in the evidence summary applied to the high-risk sub-group of patients under consideration. The health economist expressed a lack of certainty around the reported reduction of the ICER to below £20,000 with the reduced cost of bevacizumab as the model was not available. Gail Woodland confirmed that the paper by Hinde et al specified that the cost-effectiveness was driven by the drug acquisition cost. A discussion ensued regarding the price of bevacizumab.

The Chair invited discussion of any budget impact issues. Members questioned whether the patient numbers expressed in the evidence summary were reflective of practice in NHS Wales, the clinical expert confirmed that this was the case.

The Chair invited discussion of patient and public perspectives and highlighted the patient summary from Ovacome. The clinical expert expressed the view that the availability of bevacizumab has a wider societal impact than individual patients. There is a wider awareness that this medicine cannot be accessed in Wales, reflecting on the country as a whole.

The Chair invited discussion around wider societal and health and care issues. The clinical expert was of the opinion that clinicians were keen to engage in data collection particularly if it were not too onerous in terms of time. The clinical expert agreed to co-ordinate start/stop criteria for use of bevacizumab if use were approved by the group.

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 24th June

Using the agreed starting and stopping criteria, bevacizumab at a dose of 7.5 mg/kg in combination with carboplatin and paclitaxel can be made available within NHS Wales for the front-line treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer

The risks and benefits of the off-label use of bevacizumab 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.

5. Minutes of the previous meeting

The draft minutes of the April IPCG meeting were checked for accuracy and confirmed. The minutes of the meeting will be made available on the AWTTC website once endorsement from the Chief Executive Management Team of the recommendations have been received.

6. Assessment

Cannabidiol (Epidyolex®) as an adjunctive treatment of seizures associated with Dravet syndrome and Lennox-Gastaut syndrome.

The Chair introduced the clinical expert, Dr Frances Gibbon. The Chair invited any declarations of interest specific to this assessment; the clinical expert stated that they had been present at a board meeting of the manufacturer GW Pharma and had sat on the cannabis-based products guidance committee of the British Paediatric Neurology Association.

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

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 clarified that currently in NHS Wales there is provision for seven patients in CAV and five patients in Swansea Bay Health Board. Members queried the discrepancy between the retention rate estimated by some clinical experts and that reported in the clinical trials. The clinical expert was of the opinion that a retention rate of 20% was an underestimate, in their experience of treating four patients to date they have a 50% retention rate. Members asked about the difference between patients with Dravet's syndrome and those with Lennox-Gastaut syndrome. The clinical expert explained that Dravet's syndrome has a specific genotype whilst the definition of Lennox-Gastaut syndrome is much broader and encompasses a potentially wide group of patients. The clinical expert stated that in their experience currently there is greater patient demand for whole cannabis extract than for the cannabidiol product, however, demand for cannabidiol is expected to increase significantly on receipt of marketing authorisation. Members questioned if the cannabidiol product had any psychoactive effects, the clinical expert confirmed that it does not. The group asked the clinical expert if they could explain the high response rate reported for the placebo arm of the GW2 clinical trial. The clinical expert was of the opinion that as the outcomes were self-reported the placebo response may reflect some bias. Members asked about the significance in drop in seizure frequency demonstrated in the clinical trial data. The clinical expert explained that a 50% reduction in seizure activity is considered efficacious. The expert did point out that seizure type is also significant, for example the tonic/clonic seizures associated with Dravet's syndrome can be more dangerous than other seizure activity.

The Chair invited discussion on cost-effectiveness issues. The health economist was of the opinion that the cost effectiveness model provided by the company was good, however, but expressed reservations regarding the input data. They did highlight that as an orphan/ultra-orphan treatment this is not unexpected but it has resulted in considerable uncertainty with an ICER range from between approximately £20,000 to £80,000. Clarity around the dose was sought. The clinical expert confirmed that they would expect to use 10 mg/kg per day or below. To compensate for the small number of patients the visual analogue scale had been extrapolated. The group questioned the use of patients to generate utilities rather than members of the public it was noted that this is an unusual approach and also there is no EQ5D data, possibly because the patient group was predominantly children.

A discussion around the current early access programme ensued. The clinical expert informed the group that if a patient receives cannabidiol through the access programme and discontinues treatment another patient cannot be started on treatment in their place. The health economist highlighted that the UK list price for the medicine was still unknown.

The Chair invited discussion on the budget impact. Gail Woodland confirmed that a dose of 10 mg/kg in a mix of adult and paediatric patients had been used and that the budget impact is driven predominantly by cost. The group discussed the uncertainty and limitations around the model in the absence of a cost from the company. The medicine would be prescribed by specialists in hospitals and also be subject to VAT. The clinical expert highlighted the additional liver function test monitoring required every time the dose of cannabidiol is changed. Additional monitoring may require an increase in training, clinic time and specialist nurses. The Chair asked if the anticipated date of license is known. Gail Woodland informed members that the Marketing Authorisation date had been delayed and is not known at the moment. The orphan/ultra-orphan table provided in the report was discussed, the group were advised that greater uncertainty around clinical and cost-effectiveness may be accepted for orphan or ultra-orphan medicines. The group further discussed the implications of the One Wales decision in relation to commissioning advice from NHS England.

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 24th June 2019

Cannabidiol (Epidyolex®) cannot be made available within NHS Wales as an adjunctive treatment of seizures associated with Dravet syndrome and Lennox-Gastaut syndrome.

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

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