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

Interim Pathways Commissioning Group (IPCG)

Minutes of the meeting held Monday 28 January 2019 in the Board Room, University Hospital Llandough, Cardiff CF64 2XX

Members in attendance:
Sharon Hopkins, Director of Transformation and Informatics, C&V, IPCG Chair
Alan Clatworthy, Clinical Effectiveness and Formulary Pharmacist, ABMU
Ian Campbell, Hospital Consultant C&V, NMG representative
Rick Greville, Director of ABPI Wales
Fiona Woods, Director, WMIC, C&V
Andrew Champion, Assistant Director, Evidence Evaluation, IPFR representative WHSSC
Brian Hawkins, Chief Pharmacist, Medicines Management, Cwm Taf
Will Oliver, Assistant Director of Therapies and Health Science, Hywel Dda
Bethan Tranter, Chief Pharmacist, Velindre Trust
Jonathan Simms, Clinical Director of Pharmacy, Aneurin Bevan

Via teleconference:
Bernadette Sewell, Health Economist, Swansea University
Stuart Bourne, Deputy Director Public Health, Powys

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
Stuart Keeping, Senior Appraisal Scientist
Clare Elliott, Senior Appraisal Scientist
Jessica Davis, Medical Writer
Laura Phillips, Administration Assistant
Alice Varnava, Medical Writer
Bridget-Ann Kenny, Medical Writer

Clinical experts:
Dr Louise Hanna, Consultant Clinical Oncologist, Velindre
Dr Sandip Raha, Consultant in medicine and care of the elderly, ABMU

Patient organisation:
Rachel Williams, Policy, Campaigns and Communications Manager, Parkinson's UK Cymru

List of Abbreviations:

ABMU	Abertawe Bro Morgannwg University
ABPI	Association of the British Pharmaceutical Industry
AWPAG	All Wales Prescribing Advisory Group
AWTTC	All Wales Therapeutics & Toxicology Centre
CHC	Community Health Council
C&V	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
Debra Fitzsimmons, Health Economist, Health Outcomes, WHESS
James Coulson, Clinical Pharmacologist, C&V

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 asked to ensure they had signed and returned the confidentiality statements to AWTTC. The Chair invited any declarations of interest; there were none.

4. Assessment 1
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 at high risk for progression.

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.

Gail Woodland presented the key aspects of the review document.

The Chair introduced the clinical expert, Dr Louise Hanna. 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 thanked the clinical expert and colleagues for providing IPCG with a letter supporting the use of bevacizumab for the indication under consideration, highlighting its clinical effectiveness, the unmet need and its availability in England and Scotland.

The clinical expert sought clarification on the purpose of the review. The Chair clarified that the committee would be considering whether there is significant new information available to justify a full re-assessment of the One Wales decision, or whether the current decision should remain unchanged. The Chair invited the clinical expert to provide the committee with an overview of the clinical context. The clinical expert highlighted that evidence shows that bevacizumab is clinically effective and based on its mechanism of action it is most efficacious in patients with residual disease. The clinical expert discussed the evidence for its use in stage IV disease. Bevacizumab is well tolerated and patients in the high-risk group have a slightly better quality of life. The clinical expert noted that the majority of patients in the UK have access to bevacizumab for this indication, as it is available on the Cancer Drugs Fund in England and the Scottish Medicines Consortium has recommended its use at the licensed dose (15 mg/kg). Patients in Wales are aware of the inequity of access. The clinical expert also highlighted that patients in Wales are being denied access to clinical trials as a

result of the negative One Wales decision. The number of patients receiving bevacizumab has rapidly decreased since the One Wales decision, and the medicine is rarely given now. The clinical expert noted that patients with stage IV disease have a life expectancy of less than two years and therefore the National Institute for Health and Care Excellence's (NICE) criteria for appraising life-extending, end of life treatments would apply. Clinicians in Wales have highlighted the lack of transparency in the decisions made by IPCG and without knowing why the medicine was not supported for use in Wales, they have found it difficult to explain this to patients. Prof Phil Routledge clarified that IPCG adhere to the same principles and transparency as NICE and the All Wales Medicines Strategy Group (AWMSG). To improve transparency, IPCG will be recording the rationale for all decisions going forward.

The Chair opened general discussion on the review. Members questioned whether there are any outcome data available from the Cancer Drugs Fund. The clinical expert was not aware of any outcome data. Members sought clarification on the current usage of bevacizumab for this indication in Wales and England. The clinical expert confirmed that until the One Wales decision was published in 2016, patients were accessing bevacizumab via the individual patient funding request (IPFR) process and in Abertawe Bro Morgannwg Health Board bevacizumab was listed on the formulary for this indication. Since the One Wales decision, bevacizumab has been removed from the formulary and IPFRs are rarely submitted because the majority are rejected. In England, bevacizumab is standard practice. Members highlighted that the IPFR route is still available for bevacizumab following a negative One Wales decision. Members discussed the reliability of data from conference abstracts. Gail Woodland informed members that a thorough literature search is performed, the results are sifted and any new relevant evidence is presented, acknowledging that conference abstracts are a low level of evidence and have not been peer reviewed. The committee applies relevant weighting to the new data available.

The Chair invited discussion of any cost-effectiveness issues. The health economist highlighted that an incremental cost-effectiveness ratio (ICER) of approximately £48,000 per quality-adjusted life-year (QALY) gained would likely result in a loss of two to four QALYs elsewhere in the service.

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

Date of original advice: Friday 27 May 2016
Date of review: Monday 28 January 2019

It is the view of the Interim Pathways Commissioning Group (IPCG) that bevacizumab (Avastin®) 7.5 mg/kg in combination with carboplatin and paclitaxel should continue to not be supported within NHS Wales for the front-line treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer at high risk for progression. High risk is defined as: International Federation of Gynaecology and Obstetrics [FIGO] stage III debulked but residual disease more than 1.0 cm or stage IV disease, or stage III disease at presentation and requiring neoadjuvant chemotherapy due to low likelihood of optimal primary surgical cytoreduction.

5. Assessment 2

Opicapone (Ongentys®▼) as an adjunctive therapy to preparations of levodopa/DOPA decarboxylase inhibitors in adult patients with Parkinson's disease and end-of-dose motor fluctuations who cannot be stabilised on those combinations.

The Chair invited any declarations of interest specific to this assessment. The clinical expert informed the group that he had received funding from the company to attend a conference. No other interests were declared.

Rosie Spears presented the key aspects of the evidence status report. Rosie Spears confirmed that the marketing authorisation holder has agreed to make a full health technology assessment submission to AWMSG within 12 to 18 months.

The Chair introduced the clinical expert, Dr Sandip Raha. 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 introduced the patient organisation representative, Rachel Williams. The Chair described the role of the patient organisation representative 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 patient/carer perspective. The Chair highlighted that patient organisation representatives should relay broad views of the organisation and should not express personal opinion.

The Chair invited the clinical expert to provide the committee with an overview of the clinical context. The clinical expert noted that there are 12 to 14 patients in his health board receiving opicapone treatment following their involvement with the clinical trial. Opicapone is better tolerated and has fewer side effects than Stalevo® (levodopa, carbidopa and entacapone). Stalevo® is most commonly prescribed in NHS Wales. Stalevo® is difficult to swallow. If the active ingredients are taken separately this increases the tablet burden. Some patients with Parkinson's disease have incontinence and drool saliva, and entacapone is excreted in bodily fluid as a bright orange colour. The clinical expert noted that opicapone has not been in clinical use for very long, therefore the duration of treatment is unknown.

The Chair invited the patient organisation representative to provide the committee with an overview of the patient perspective. The patient organisation representative presented feedback from patients approximately 70 years of age, who have had Parkinson's disease for around 10 years and are receiving opicapone treatment. Patients noted that opicapone is having a positive impact on their lives and is improving their quality of life when in the on state. Patients highlighted the benefit of one tablet a day and noted that they have not experienced diarrhoea and weight loss, which they had done with entacapone.

The Chair opened general discussion in relation to clinical effectiveness. Members sought clarification on the patient population included in the BIPARK studies. The clinical expert confirmed that the trials included patients from Western Europe. Members asked the clinical expert about the current use of tolcapone in clinical practice. Tolcapone is associated with an increased risk of hepatic toxicity. The clinical expert confirmed that very few patients receive treatment with tolcapone. He noted that patients often prefer to not receive tolcapone due to the associated blood tests and monitoring required. It was discussed that if opicapone were to be supported for use,

tolcapone would move to third line in the treatment pathway due to the increased adverse effects associated with tolcapone. Members asked the clinical expert how long would patients receiving opicapone be under specialist care before transferring to primary care. The clinical expert confirmed that three months under specialist care would likely be sufficient given that opicapone is a licensed medicine and it does not require any monitoring. Members asked about the availability of opicapone in Scotland. Gail Woodland confirmed that the company has not made a submission to the Scottish Medicines Consortium. Members questioned the strength of commitment for the company to submit to AWMSG for full health technology assessment. Gail Woodland confirmed that the company understand that any One Wales decision is contingent on a submission and this will be made explicit in any forthcoming advice. Members questioned the collection of outcome data. It was noted that the company and clinicians are working together to gather outcome data. Gail Woodland informed the group that any recommendation would include agreed start and stop criteria.

The Chair invited discussion of any cost-effectiveness issues. The health economist noted that it is very difficult to support the use of opicapone without any health economic evidence. The health economist noted that there is no quality of life data and although it would be conceivable that the ICER would be favourable, it is based on large assumptions and not supported by data. Gail Woodland highlighted that the company's economic study is currently going through ethics approval.

The Chair invited discussion of any budget impact issues. Members discussed that opicapone would delay, rather than prevent, apomorphine treatment. Members noted the small difference in cost between Stalevo® and opicapone.

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

Date of advice: Monday 28 January 2019

Using the agreed starting and stopping criteria opicapone (Ongentys®▼) can be made available within NHS Wales as an adjunctive therapy to preparations of levodopa/DOPA decarboxylase inhibitors in adult patients with Parkinson's disease and end-of-dose motor fluctuations who cannot be stabilised on those combinations. Opicapone is restricted for use only after failure of entacapone, or in patients who cannot tolerate entacapone or have concordance issues. This recommendation applies only in circumstances where the approved commercial arrangement price is applied. Advice is conditional on subsequent Health Technology Assessment advice from AWMSG or NICE becoming available.

6. Date of next meeting

The Chair confirmed that the next meeting on 25 February 2019 would be a virtual consultation for one review.

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