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

# Interim Pathways Commissioning Group (IPCG)

## Minutes of the meeting held Monday 27th November 2017 in the Academic Centre, University Hospital Llandough, Cardiff CF64 2XX

**Members in attendance:**
Alan Clatworthy, Clinical Effectiveness and Formulary Pharmacist, ABMU, IPCG Chair
Ian Campbell, Hospital Consultant C&V, NMG representative
Rick Greville, Director of ABPI Wales
Geoff Greaves, CHC representative
Fiona Woods, Director, WMIC, C&V
Stuart Davies, Finance Director, WHSSC
Andrew Champion, Assistant Director, Evidence Evaluation, IPFR representative WHSSC
Simon Waters, Consultant Oncologist, Velindre Trust
Brian Hawkins, Chief Pharmacist, Medicines Management, Cwm Taf
Will Oliver, Assistant Director of Therapies and Health Science, Hywel Dda

**Via teleconference**:
Debra Fitzsimmons, Health Economist, Health Outcomes, WHESS
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
Jessica Davis, Medical Writer
Laura Phillips, Administration Assistant

**Clinical experts:**
Dr Louise Hanna, Consultant Clinical Oncologist, Velindre

**List of Abbreviations:**

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| 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

Sharon Hopkins, Director of Public Health, C&V
Sue Jeffs, Hospital Consultant AB, AWPAG representative
Jonathan Simms, Clinical Director of Pharmacy, Aneurin Bevan
Marysia Hamilton-Kirkwood, Assistant Medical Director of Public Health, Aneurin Bevan
Bethan Tranter, Chief Pharmacist, 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 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.

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 evidence status report (ESR).

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 opened general discussion in relation to clinical effectiveness. The clinical expert sought clarification on the indication and questioned whether IPCG would consider subgroups of the indication. The assessment lead confirmed the indication: bevacizumab at a dose of 7.5 mg/kg for those patients deemed to be high-risk for progression: patients with 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. The assessment lead added that it would be down to IPCG to decide whether to consider subgroups of the indication.

The members considered the number of cycles of treatment (i.e. 18 cycles) and sought reassurance that this would be adhered to. The clinical expert noted that on average most patients would receive less than 18 cycles of treatment and if a patient's disease progresses whilst receiving bevacizumab, the treatment would be stopped. The clinical expert was not aware of any centres which do not adhere to 18 cycles of treatment. Members asked the clinical expert whether the dose of bevacizumab would be increased to 15 mg/kg for patients whose disease progresses whilst receiving the 7.5 mg/kg dose. The clinical expert confirmed that the dose would not be increased to 15 mg/kg as the ICON7 study showed similar efficacy between the 7.5 mg/kg and 15 mg/kg doses. The assessment lead highlighted to members patient outcome data received from one cancer centre in Wales that provided data on average treatment duration. .

Members discussed the safety profile of bevacizumab. ICON7 reported safety data for the whole study population. The data were not divided by subgroups. Data for high-risk patients are reported in the South West Wales study. The clinical expert highlighted the unpublished safety data from South East Wales. The most toxic adverse event reported was hypertension grade 2–3 which is manageable. There was no other grade 3 or 4 toxicity reported.

Members sought clarification on the indication being considered as there were no data presented for fallopian tube and peritoneal cancer. The clinical expert confirmed that ovarian, fallopian tube and peritoneal cancer are considered together as one entity.

The Chair invited discussion of any cost-effectiveness issues. The health economist confirmed that the cost-effectiveness data presented in the ESR was a fair reflection of the paper by Hinde et al (2016). The All Wales Medicines Strategy Group (AWMSG) end of life policy was discussed. Members noted the criteria supporting the policy. Part of the criteria refers to patients having a life expectancy of less than 24 months. It was noted that the median overall survival of patients in the high-risk subgroup in the chemotherapy alone arm of the ICON7 study was 30.2 months.

Members discussed the cost of adverse events. The clinical expert highlighted that most adverse events are low grade and not costly e.g. hypertension and proteinuria. The assessment lead noted that adverse events are not included in the budget impact. Members noted that the cost of treating adverse events were included in the health economic model. This was confirmed by the health economist. Members questioned the significance of the health economic model not being available for review. The health economist highlighted that the analyses were thorough and several sensitivity analyses had been performed to address uncertainty and that the published paper was commensurate with good practice.

Members discussed the quality of life data presented in the ESR. Although a small increase in the quality of life scores was shown for high-risk patients who received bevacizumab in the ICON7 study, it was not statistically significant compared to the control group. The clinical expert reassured members that patients do not have a worse quality of life with bevacizumab treatment compared to chemotherapy alone.

Members sought clarification on the certainty of patient numbers in Wales assumed to be eligible for treatment with bevacizumab. The assessment lead confirmed that this figure was provided by clinical experts.

The Chair invited discussion on the patient and public perspective. Members questioned whether the ICON8b study is company sponsored. The clinical expert confirmed that the study is not company sponsored. The clinical expert added that ICON8b is an international study and bevacizumab 7.5 mg/kg is the control treatment. Patients in Wales are not being recruited on to this trial as bevacizumab 7.5mg/kg is not routinely available in NHS Wales.

The Chair invited discussion on any wider societal issues. Members questioned the life expectancy of patients with stage IV disease. The clinical expert noted that there is a difference in the survival rates of patients with stage III and IV disease. An International Federation of Gynaecology and Obstetrics (FIGO) 2006 survival curve showed that median survival at stage IV is two years. Members discussed the Scottish Medicines Consortium's appraisal of bevacizumab 15 mg/kg which was restricted to stage IV disease. It was noted from the GOG-0218 study that the overall survival of patients with stage IV disease was approximately 40 months. However, it was highlighted that patients in this study had better performance status than the real word.

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 27th November 2017**

It is the view of the Interim Pathways Commissioning Group (IPCG) that bevacizumab (Avastin®) at a dose of 7.5 mg/kg in combination with carboplatin and paclitaxel should 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**

**Arsenic trioxide (TRISENOX®)** in combination with all-trans retinoic acid for the treatment of acute promyelocytic leukaemia in adult patients unsuitable for anthracycline-based therapy.

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

Rosie Spears presented the key aspects of the review document. Rosie Spears confirmed that the marketing authorisation holder has agreed to make a submission to AWMSG for health technology assessment of the licensed part of the indication.

The Chair opened general discussion on the review. Members asked about the timelines of the technology appraisal of the licensed indication by NICE. The assessment lead confirmed that the appraisal is proposed but is not yet in progress. Members asked whether the license is going to be extended for high-risk acute promyelocytic leukaemia. The assessment lead was not aware of a licence extension.

Proceedings were concluded by the Chair and members were asked to vote. The IPCG recommendation for health boards Chief Executives was agreed:

**Date of original advice: Monday 26th September 2016**
**Date of review: Monday 27th November 2017**

Arsenic trioxide (TRISENOX®) in combination with all-trans retinoic acid can continue to be made available within NHS Wales for the first line treatment of acute promyelocytic leukaemia (APL) in adult patients unsuitable for anthracycline-based therapy.

**6. AOB**

Gail Woodland informed the group that AWTTC will be sending out the current list of IPCG members and asked the group to check that the list is correct, deputy members would be recruited into vacancies.

Rosie Spears provided outcome data for patients treated for uveitis with adalimumab following the One Wales decision.

**7. Date of next meeting**

The Chair confirmed the next meeting would be held on Monday 29th January 2018 in Cardiff.

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