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 26 October 2020

Members in attendance:
John Watkins, Consultant in Public Health, IPCG Chair
Sue Beech, Clinical Development Pharmacist, Hywel Dda
Ian Campbell, Hospital Consultant CAV, NMG representative
Andrew Champion, Assistant Director, Evidence Evaluation, IPFR representative WHSSC
Alan Clatworthy, Clinical Effectiveness and Formulary Pharmacist, Swansea Bay
Jo Ferris, Operations Manager, ABPI Cymru Wales
Debra Fitzsimmons (Health Outcomes), Welsh Health Economics Support Service
Teena Grenier, Medicines Governance Lead, Betsi Cadwaladr
Marysia Hamilton-Kirkwood, Assistant Medical Director – Public Health
Brian Hawkins, Chief Pharmacist, Medicines Management, Cwm Taf Morgannwg
Malcolm Latham, Community Health Council

AWTTC:
Karen Samuels, Head of Health Technology Appraisal
Rob Bracchi, Medical Director
Gail Woodland, Senior Appraisal Pharmacist
Jessica Davis, Senior Appraisal Scientist
Rosie Spears, Senior Appraisal Scientist
Bridget-Ann Kenny, Medical Writer
Katherine Chaplin, Medical Writer
Laura Phillips, Admin Supervisor

Clinical experts:
Dr Nachi Palaniappan, Consultant Oncologist, 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
Jonathan Simms, Clinical Director of Pharmacy, Aneurin Bevan
Hywel Pullen, Finance Director, Cardiff and Vale
Berni Sewell, Health Economist, Swansea University
William King, Consultant in Public Health, Powys

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 18 May (Zoom) as well as endorsement of reviews considered virtually in January, June and July 2020

- azacitidine for treatment of relapsed angio-immunoblastic T cell lymphoma
- review of adalimumab for treatment of paediatric patients with severe refractory non-infectious intermediate, posterior and pan-uveitis
- review of arsenic trioxide in combination with all-trans retinoic acid for the first-line treatment of high-risk acute promyelocytic leukaemia in adult patients unsuitable for anthracycline-based therapy
- review of bendamustine in combination with rituximab for the treatment of previously untreated and relapsed mantle cell lymphoma and indolent lymphomas
- review of bevacizumab 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

Chief Executive Management Team endorsement is pending for the August 2020 reviews of rituximab for treatment of interstitial lung disease and for myasthenia gravis and denosumab for treatment of osteoporosis in men.

The Chair announced that since the previous meeting, AWMSG has received a submission from Bial Pharma UK Ltd for the assessment of opicapone (Ongentys®) as an adjunctive therapy to preparations of levodopa/DOPA decarboxylase inhibitors (DDCI) in adult patients with Parkinson's disease and end-of-dose motor fluctuations who cannot be stabilised on those combinations. In January 2019, IPCG assessed opicapone and supported its use interim to HTA advice.

The recommendation from today's meeting will be forwarded to the Chief Executive Management Team for their consideration on 17 November 2020.

5. Re-assessment

Abiraterone, enzalutamide and apalutamide for the treatment of hormone-sensitive prostate cancer during the COVID-19 pandemic

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.

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

The Chair introduced the clinical expert, Dr Nachi Palaniappan. 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 explained that since the One Wales advice for the treatment of hormone sensitive prostate cancer during the COVID pandemic was published in April, abiraterone, enzalutamide and apalutamide have been given to patients who would have otherwise been suitable for treatment with docetaxel in line with the NICE guidelines. The majority of patients have high-risk metastatic HSPC with the exception of a couple of patients with locally advanced HSPC with multiple nodes. The clinical expert stated that the use of enzalutamide and abiraterone are currently being favoured, primarily on grounds of cost as all three medicines have similar efficacy in terms of overall survival.

The Chair opened general discussion relating to the clinical effectiveness of the three medicines. Members requested confirmation on the patient population, and place in the treatment. The clinical expert confirmed that these medicines were being prescribed instead of docetaxel in this group of patients mirroring docetaxel use as recommended in the NICE guideline. Members asked if enzalutamide was the first line choice for these patients. The clinical expert explained that for younger patients with fewer co-morbidities then enzalutamide would be first choice and then if patients were intolerant to treatment they would be switched to abiraterone. Abiraterone may be favoured in particular patient groups based on potential drug interactions and co-morbidities. Members asked about the differences in monitoring for patients, the clinical expert explained that monitoring for abiraterone is recommended every two weeks for three months and monthly thereafter. For enzalutamide monthly monitoring is routine.

Members asked about the validity of study results where participants had been treated with apalutamide or enzalutamide following prior treatment with docetaxel, in particular in TITAN and ARCHES. Jessica Davis highlighted that subgroup analyses demonstrated little difference in overall survival and progression free survival associated with prior use of docetaxel. The clinical expert pointed out that similar findings were reported in STAMPEDE for abiraterone. Members asked why results for docetaxel treatment had not been included in the evidence status report tables, Gail Woodland explained that for the purposes of this assessment, docetaxel is not a valid treatment option for patients in the current COVID-19 climate and therefore has not been offered as a comparator.

The Chair invited the health economist to comment on the cost-effectiveness evidence provided. The health economist was of the opinion that the cost-effectiveness model provided by SMC which compared treatment with abiraterone in combination with ADT to treatment with ADT alone was reasonable. Using the commercial arrangement price in Wales the ICERs fell within £20,000 to £30,000. The use of a qualitative approach was thought to be the best approach considering the uncertainties associated with current use under COVID conditions. Gail Woodland explained that the SMC model had been provided to AWTTC by the company as the company deemed it easier to use. The health economist did point out that there were considerable uncertainty as the models were based on chemotherapy ineligible patients not relating to the COVID-19 situation.

The Chair invited discussion on the budget impact. Members queried the prices used for calculating the annual treatment cost of enzalutamide. Jessica Davis confirmed that the cost included an initial discounted rate plus a further reduced cost which applies from August. The Chair queried if there was any clarification available as to what would be considered the end point for commercial arrangements offered during the CIVID-19 pandemic. Gail Woodland explained that there is NICE advice pending for the use of abiraterone, expected in January 2021 and that enzalutamide and apalutamide are

currently on the NICE work programme. NICE advice supersedes a One Wales decision. AWTTC will continue to monitor the situation going forward.

Members queried why only 200 patients were expected to receive treatment in the year. This was based on an initial switch of patients from docetaxel to oral therapy, going forward only newly diagnosed patients are expected to receive treatment so the numbers will be fewer. The clinical expert explained that the high risk patients are still being diagnosed and there has not been a reduction in patient numbers. It may be that fewer biopsies are being performed on the low or median risk patients but this will not impact the patient group of interest and a surge in numbers is not expected.

The Chair invited discussion on the patient and public perspective. The clinical expert informed the group that patients are thankful to not have to attend hospital during the pandemic. Consultations are made virtually and blood samples for monitoring are taken at GP surgeries. Medication is delivered to the patient's home. The quality of life is reduced in the short term as side effects of the medication are apparent in the early stages of treatment. Potential side effects of treatments were discussed.

The Chair invited discussion on the wider societal and health and social care issues. Members asked about equity of access to these medicines across all three cancer centres in Wales based on initial uptake figures. There appeared to be reassurances that this initial difference was levelling out. AWTTC will continue to monitor uptake and the group agreed to review the recommendation in 6 months, where uptake would be reviewed. Members were asked to note the data from the National prostate cancer audit which had also been used to extrapolate the likely number of patients in Wales and was in line with the AWTTC patient number estimates.

Members asked about the duration of treatment and follow up protocols. The clinical expert explained that for treatment of metastatic HSPC patients would be until disease progression. For locally advanced, node positive disease treatment is continued for two years. Members asked what treatment patients will receive once the COVID-19 pandemic is over. The clinical expert advised that it would depend upon NICE recommendations at the time, if the oral therapies were not available then treatment with docetaxel would resume. The option of available licensed medicines was discussed.

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 26 October

Using the agreed starting and stopping criteria, enzalutamide (Xtandi®) can be made available within NHS Wales for the treatment of high-risk locally advanced, and metastatic hormone-sensitive prostate cancer during the COVID-19 pandemic. Abiraterone acetate (ZYTIGA®) can be made available for patients who are intolerant of enzalutamide or where enzalutamide is deemed to be unsuitable. These recommendations apply only in circumstances where the approved commercial arrangement prices are applied.

Abiraterone (ZYTIGA®) is licensed for the treatment of newly diagnosed high-risk metastatic hormone-sensitive prostate cancer in adult men in combination with androgen deprivation therapy. For the licensed indications, this One Wales Interim Commissioning decision is interim to subsequent Health Technology Assessment advice from AWMSG or NICE becoming available.

Enzalutamide (Xtandi®) is not licensed to treat these indications, abiraterone (ZYTIGA®) is not licensed to treat low-risk metastatic disease or high-risk locally advanced disease. Each provider organisation must ensure all internal governance arrangements are completed before these medicines are prescribed. The risks and benefits of the off-label use of these medicines for these indications should be clearly stated and discussed with the patient to allow informed consent. Providers should consult the relevant guidelines on prescribing unlicensed medicines before any off-label medicines are prescribed.

It is the view of the Interim Pathways Commissioning Group (IPCG) that apalutamide (Erleada®) should not be supported within NHS Wales for the treatment of these indications. Patients who are currently receiving apalutamide (Erleada®) should have the option to continue therapy until they and their consultant consider it appropriate to stop.

This advice will be reviewed after 6 months or earlier if new evidence or information becomes available.

6. Minutes of the previous meeting

The draft minutes of the May 2020 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. Next meeting

The Chair confirmed that the next meeting will be on 23 November 2020. The Chair then thanked members for their participation and closed proceedings.