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

One Wales Medicines Assessment Group (OWMAG)

Minutes of the virtual (Teams) meeting held Monday 26 September 2022

Members in attendance:
Andrew Champion, Assistant Director, Evidence Evaluation, OWMAG Chair
Alan Clatworthy, Clinical Effectiveness and Formulary Pharmacist, representative Swansea Bay
Joe Ferris, Operations Manager, ABPI Cymru Wales
Teena Grenier, Medicines Governance Lead, representative Betsi Cadwaladr
Kathryn Howard, Head of Pharmacy, Royal Glamorgan Hospital, representative Cwm Taf Morgannwg
Malcolm Latham, Community Health Council, Lay representative
Hywel Pullen, Director of Finance, WHSSC
Berni Sewell, Senior Lecturer, Health Economist, Swansea University
Jonathan Simms, Clinical Director of Pharmacy, representative Aneurin Bevan
Michael Thomas, Consultant in Public Health, representative, Hywel Dda
William King, Consultant in Public Health, representative Powys

AWTTC:
Tony Williams, Senior Appraisal Pharmacist, Team Leader
Gail Woodland, Senior Appraisal Pharmacist
Clare Elliott, Senior Appraisal Scientist
Rachel Jonas, Medical Writer
Laura Phillips, Admin Supervisor

Clinical experts:
Dr Jacob Tanguay, Consultant Oncologist, Velindre University NHS trust
Dr Rachel Rayment, Consultant Haematologist, Cardiff and Vale NHS Health board

List of Abbreviations:

ABPI	Association of the British Pharmaceutical Industry
AWTTC	All Wales Therapeutics & Toxicology Centre
CEMT	Chief Executive Management Team
ESR	Evidence Status Report
IPFR	Independent Patient Funding Request
NICE	National Institute for Health and Care Excellence
NMG	New Medicines Group
OWMAG	One Wales Medicines Assessment Group
SPC	Summary of Product Characteristics
WHSSC	Welsh Health Specialised Services Committee

1. Welcome and Introduction

The Chair opened the meeting and welcomed members.

2. Apologies

John Watkins, Consultant in Public Health, Chair (Andrew Champion deputy Chair, chaired the meeting in John Watkins' absence)
Ian Campbell, Hospital Consultant CAV, NMG representative
Richard Hain, Consultant in Paediatric Palliative care, representative, Cardiff and Vale
Bethan Tranter, Chief Pharmacist, Velindre Trust

3. Declaration of Interests/Confidentiality

The Chair reminded members that all OWMAG 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 informed members that since the last virtual meeting we have received endorsement from the Chief Executive Management Team (CEMT) for the medicine considered at the last meeting in March 2022 (sorafenib for maintenance treatment following allogeneic stem cell transplantation for acute myeloid leukaemia associated with a FLT3 ITD mutation).

CEMT endorsement has also been received for reviews considered virtually in March 2022, mepolizumab for the treatment of chronic eosinophilic pneumonia and rituximab for the treatment of pemphigus (excluding pemphigus vulgaris) and pemphigoid disease. These are displayed on the AWTTC website and the service has been informed.

To date AWTTC have performed 6 reviews (4 internally) in 2022, there are an additional 4 reviews for consideration by OWMAG in October and December this year. An overview was given for the upcoming assessments due later in the year and preferences for meetings.

The recommendations from today's meeting will be forwarded to the Chief Executive Group for their consideration on 18 October 2022.

5. Assessment one

Abiraterone acetate for the treatment of non-metastatic, high-risk, hormone-sensitive prostate 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.

The Chair introduced the clinical expert, Dr Jacob Tanguay. The Chair described the role of the clinical expert as an invited observer of the OWMAG 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 the intent of treatment in this patient population is potentially curative. Therefore, an improvement in overall survival/progression free survival will reduce the need for these patients to access downstream treatments. It is important to note if patients relapse after this potentially curative treatment, there are other very expensive treatment options available so if we can increase their chance of cure, then potentially we get a cost saving.

The clinical expert confirmed oncologists in Wales are very comfortable with the STAMPEDE definition eligibility criteria for abiraterone and the UK recruited a high percentage of patients to the trial. In terms of the duration of treatment, 2.5 years is a reasonable estimate which is reflected in the budget impact section. It is worth noting that there is an overlap of patient groups in the evidence - Attard et al. overlaps with James et al., however Attard has much more recent data, which highlights the improvement of overall survival benefits.

The Chair opened general discussion relating to the clinical effectiveness of abiraterone.

Members asked what the uptake and response is to abiraterone acetate in clinical practice. The expert stated that abiraterone is generally very well tolerated and most of its side effects are very similar to the Prostap injections that patients get anyway. Hypertension is noted which is easily treated and there is monitoring of liver function but any elevations can be treated with a

dose reduction. The level of monitoring recommended in the SPC may be higher than is undertaken in clinical practice. Docetaxel in contrast can cause alopecia leading to body image issues. There is a risk of sepsis neutropenia with docetaxel, which can be fatal. In his clinical experience very few have chosen docetaxel (10%) over abiraterone (90%).

It was queried if there was a 2.5 year stopping criteria applied, and various downstream medicines available, should reintroduction of an Androgen Receptor Targeted Agent (ARTA) be considered? It was confirmed this would be offered, in accordance with previous response to treatment, and is now considered standard therapy.

The Chair invited the health economist to comment on the cost-effectiveness evidence provided. The health economist highlighted the absence of any cost-effectiveness analyses for the comparison of abiraterone acetate versus docetaxel.

The group agreed that the STAMPEDE population with non-metastatic disease reflects the Welsh population appropriately. The prices used in the model were based on list prices of the product available at the time of the analyses, however generic abiraterone will be available from October 2022. The model is robust and well-designed using data from the STAMPEDE trial.

In the model, the QALY gain is fairly small, but if there is more benefit as suggested by clinical experts this will increase cost effectiveness. However, this is based on several assumptions. The group were reminded there is no direct comparison to docetaxel available. If the clinical efficacy of abiraterone is assumed to be non-inferior to docetaxel then the cost of the two treatments would need to be considered. A discussion ensued around costs. It was highlighted that the Woods paper was included to highlight the similar QALY gains between docetaxel and abiraterone. It was confirmed if approved, patients will be offered a choice of both treatments.

The uptake of docetaxel across cancer centres in Wales was discussed. It was noted that various scenarios were included in the budget impact to account for potential differences in uptake, ranging from 40 to 70%. The impact of different patient numbers was also presented. The clinical expert confirmed that Velindre was one of the largest recruiting centres internationally to STAMPEDE. As abiraterone is an oral therapy, making abiraterone available as an option might increase accessibility for patients who would otherwise have to travel to receive their chemotherapy. No consideration of sequential therapy was highlighted as a limitation of the budget impact. It was confirmed that any One Wales advice would apply equally to the generic formulations of abiraterone acetate.

The Chair invited discussion on the wider societal and health and social care issues. No questions were raised.

6. Assessment two

Vonicog Alfa (Veyvondi®) for the treatment of surgical (elective and emergency) bleeding episodes in children aged up to 17 years with severe von Willebrand disease.

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.

Clare Elliott presented the key aspects of the evidence status report.

The Chair introduced the clinical expert, Dr Rachel Rayment. The Chair described the role of the clinical expert as an invited observer of the OWMAG 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 there may have some miscommunication regarding patient numbers. There are about 60 paediatric patients with the condition in Wales, of which approximately 5 or 6 patients this year would have been eligible for treatment.

The intended use of vonicog alfa was also queried. The population should also include patients presenting with a bleeding episode caused by an accident or a cut but not requiring surgery, as well as somebody who presents requiring emergency surgery and all elective surgery.

The expert was asked if the indication could be expanded further than what is presented in the ESR to match the adult commissioning criteria published by WHSSC. It was agreed this is within scope and that the budget impact presented can be used as the net impact is provided. There is no further clinical evidence to include for this expanded population.

It was acknowledged by the group that there are sparse data available and asked how applicable was the transition of evidence from adults to paediatrics? The clinical expert confirmed that there were no concerns as all dosing is based on body weight and pharmacokinetics are known, so titration is against laboratory levels. The differences in molecular levels between vonicog alfa and plasma derived product were also discussed.

The Chair invited the health economist to comment on the cost-effectiveness evidence provided. The health economist highlighted the absence of any cost-effectiveness analyses. The health economist highlighted the main cost difference comes from the additional need of factor VIII. The medicine cost will vary as dosing is weight based but there is unlikely to be a significant net cost increase. The clinical expert confirmed a child is more likely to need factor VIII than an adult, but the cost of Advate® has reduced significantly over the years.

The expert was asked if there are data for clinical safety due within the next 18 months why are we not waiting for this before deciding. The clinical expert believed if a child were to receive a dose of plasma derived product in the next 18 months (as a one in a lifetime exposure) when there is a recombinant product available which is already licenced in adults, then there is an opportunity to reduce the risk of transfusion transmitted infection by making vonicog alfa available now through One Wales. The clinical expert also confirmed that patients with VWD will be managed in coordination with the specialist service at UHW to assist on dosing etc. Vonicog alfa is ordered from the Welsh Blood Service and it is prescribed on specialist advice.

The Chair invited discussion on the patient and public perspective. It was highlighted that the cost is low and the patient group is small. The inequity of access compared with adults was highlighted especially with the potential associated risks with currently available treatment options for children. This raised ethical concerns as to the potential exposure risk for children, who would be treatment-naïve, versus adults who may have prior exposure to plasma derived products but who were able to access vonicog alfa through commissioning advice in Wales.

It was noted that as this is a blood product it is excluded from AWMSG remit. WHSSC will commission based on the interim One Wales decision. WHSCC has also confirmed continued commissioning when licenced.

The group discussed broadening the indication to match what is currently commissioned by WHSCC in adults. It was agreed the paediatric indication duplicate this and will also not include prophylaxis (which is currently not WHSCC commissioned) but is available via IPFR if access is required.

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

Date of advice: Monday 26 September

Using the agreed starting and stopping criteria, abiraterone acetate can be made available within NHS Wales for the treatment of newly diagnosed non-metastatic and locally advanced, high-risk, hormone-sensitive prostate cancer. The risks and benefits of the off-label use of abiraterone acetate for this indication 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.

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

Date of advice: Monday 26 September

Using the agreed starting and stopping criteria, vonicog alfa (Veyvondi®) can be made available within NHS Wales for on-demand treatment of non-surgical and surgical (elective and emergency) bleeding episodes in children aged up to 17 years with severe von Willebrand disease. The risks and benefits of the off-label use of vonicog alfa (Veyvondi®) for this indication 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.

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

Action points

The ESR will be updated for the vonicog alfa (Veyvondi®) indication to broaden in line with the adult population as per WHSCC commissioning policy.

Include the 2.5 years stopping criteria as per STAMPEDE in the start stop criteria.

Members are reminded that they will see the full recommendations and decision tables before they are disseminated.

7. AOB

Gail informed members that there are three reviews for the October OWMAG meeting. She reminded members that AWTTC internally perform an annual review for all medicines that have been previously considered which includes checklist and literature search and may wish to consider this when deciding on the date of the next external review.