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

Interim Pathways Commissioning Group (IPCG)

Minutes of the meeting held Monday 27th March 2017 in the Boardroom, Llandough Hospital

Members in attendance:
Sharon Hopkins, Director of Public Health, C&V, IPCG Chair
Alan Clatworthy, Clinical Effectiveness and Formulary Pharmacist, ABMU
Ian Campbell, Hospital Consultant C & V, NMG representative
Joe Ferris, Operations Manager, ABPI Cymru Wales
Geoff Greaves, CHC representative
Fiona Woods, Director, WMIC, C&V
Brian Hawkins, Chief Pharmacist, Medicines Management, Cwm Taf HB
Jonathan Simms, Clinical Director of Pharmacy, AB
Andrew Champion, Assistant Director of Evidence, Evaluation and Effectiveness, IPFR representative WHSSC

Via teleconference:
Debra Fitzsimmons, Health Economist, Health Outcomes, WHESS
Teena Grenier, Medicines Governance Lead, Betsi Cadwaladr HB
Will Oliver, Assistant Director of Therapies and Health Science, HD

AWTTC:
Phil Routledge, Clinical Director
Ruth Lang, Head of Liaison and Administration
Karen Samuels, Head of HTA, AWTTC
Gail Woodland, Senior Appraisal Pharmacist
Rosie Spears, Appraisal Scientist
Carolyn Hughes, Medical Writer
Sally Streeter, Administration Assistant

Clinical experts:
Dr Eve Gallop-Evans, Consultant Clinical Oncologist, Velindre

List of Abbreviations:

AB	Aneurin Bevan
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
HB	Health Boards
HD	Hywel Dda
ICER	Incremental cost-effectiveness ratio
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

Rick Greville, Director Wales ABPI Cymru Wales
Sue Jeffs, Hospital Consultant AB, AWPAG representative
James Coulson, Clinical Pharmacologist, C&V
Stuart Davies, Finance Director, WHSSC
Stuart Bourne, Deputy Director Public Health, Powys
Bethan Tranter, Chief Pharmacist, Velindre Trust

3. Minutes of previous meeting
The draft minutes of the previous meeting were checked for accuracy and approved. It was confirmed that the minutes would be made available on the AWTTC website.

4. 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.

5. Assessment 1
Bendamustine in combination with rituximab (MabThera®) for the treatment of mantle cell lymphoma.

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; the clinical expert Dr Eve Gallop-Evans declared that she has received educational travel grants from Roche and Takeda, and advisory board honoraria from Roche, Takeda, Merck and BMS. This will be relevant to rituximab (Roche) but not bendamustine.

Rosie Spears presented the key aspects of the evidence status report (ESR). The IPCG was being asked to consider a specific patient cohort: patients with untreated and relapsed mantle cell lymphoma for whom anthracycline-based chemotherapy is unsuitable.

The Chair introduced the clinical expert, Dr Eve Gallop-Evans. The Chair described the role of the clinical experts as invited observers 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 members noted that this was a relatively rare sub-type of lymphoma but was very aggressive. Median survival rates used to be quoted as 3 years but more intensive regimens and the inclusion of rituximab therapy have transformed the outlook for mantle cell patients. More patients are able to get to second line therapy. Members raised the lack of overall survival data for bendamustine plus rituximab in treating mantle cell lymphoma. Dr Gallop-Evans said that overall survival was difficult to demonstrate in this patient population. She also said that there is no palliative treatment that will extend life expectancy of patients or improve their quality of life. The reliability of overall survival data was questioned as this may be clouded by the use of other regimens throughout the progression of the condition and maintenance rituximab.

Members noted that whilst bendamustine in combination with rituximab may not prolong life it may improve overall quality of life.

The Chair invited general discussion of any cost effectiveness issues. Members noted that no cost effectiveness data were available. No PAS was offered by the company because the combination treatment is unlicensed.

Members considered the budget impact estimates. These were based on the net annual cost (including drug and administration costs) for the 12 patients identified. No information was available on relative costs against substitution therapies, maintenance costs were excluded from the budget impact. Members agreed that the budget impact should focus only the costs of bendamustine and its administration, because alternative regimens would usually include rituximab and therefore would not represent an additional cost.

Members agreed that based on the rarity of the condition and the other therapies currently in use it was difficult to assess whether any budget impact was likely. The assessment lead commented that the availability of a rituximab biosimilar later this year will reduce the cost of the combination. It was noted that other treatment options were more expensive than the bendamustine plus rituximab combination.

The Chair invited members to discuss the patient/public perspective.. No additional patient/public perspective issues were raised.

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

Bendamustine in combination with rituximab (MabThera®) for the treatment of previously untreated and relapsed mantle cell lymphoma

Date of advice: Monday 27th March 2017

Bendamustine in combination with rituximab (MabThera®) can be made available within NHS Wales for the treatment of previously untreated and relapsed mantle cell lymphoma in patients deemed unsuitable for anthracycline-based therapy or other health technology appraisal-approved regimens.

Bendamustine in combination with rituximab (MabThera®) is not a licensed regimen to treat this indication and is therefore 'off-label'. Each provider organisation must ensure all internal governance arrangements are completed before these medicines are prescribed in combination.

The risks and benefits of the off-label use of bendamustine with rituximab (MabThera®) 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.

6. Assessment 2

Bendamustine in combination with rituximab (MabThera®) for the treatment of previously untreated and relapsed indolent lymphomas.

Gail Woodland presented the key aspects of the evidence status report (ESR). The cohort of patients likely to be eligible for treatment were summarised.

The Chair reminded members of the role of the clinical experts and confirmed that Dr Gallop-Evans would leave the meeting after the assessment and prior to the vote.

The Chair opened general discussion in relation to clinical effectiveness. The clinical expert advised that patients may get a variety of different treatments throughout the course of their disease progression.

Members discussed the patient profile for each condition as detailed in the target group and clinical expert opinions for therapies for each of the conditions were raised and discussed. Dr Gallop-Evans commented that follicular lymphoma was the largest group of patients and that the addition of rituximab has transformed life expectancy for these patients. She also said that data are expected to be published soon from the GALLIUM clinical study of obinutuzumab (Gazyva®) for the first-line treatment of follicular lymphoma. She stated that bendamustine plus rituximab is a good second-line choice for relapsed follicular lymphoma patients and that similar treatments are used for the other lymphoma subtypes.

The clinical expert pointed out that the bendamustine and rituximab combination was regarded as a good choice for second line therapy to help patients get to transplant. Members discussed the importance of avoiding treatment toxicity, and also the increased life expectancy demonstrated in the submitted study. It was noted that there was discordance between the results of the clinical study and those used in the cost-effectiveness model.

The Chair invited general discussion of any cost effectiveness issues. It was noted that the cost effectiveness paper referred to the first line treatment of indolent lymphoma only. The HE representative confirmed that the cost utility analysis in the paper was reasonable and robust. Concern was raised over the assumption in the

paper that overall survival would be greater with bendamustine and rituximab than the comparators. Despite this, members were content that the model was appropriate and noted that this treatment was cost effective using conventional thresholds.

Members considered the budget impact estimates. The assessment lead explained the budget model further and confirmed that displacement of current treatments and maintenance rituximab were not included in the costs submitted.

The lay member commented that the possible displacement of IPFR requests and comparable treatments being cost neutral may result in zero budget impact for health boards. Cohort sizes are difficult to identify because of the range of conditions covered and the different sources of health board information; it's possible that actual patient numbers differ from those estimated by AWTTC.

The assessment lead detailed how they had arrived at the estimate of patient numbers and percentages for each condition and the members were content that every effort had been made to provide plausible and robust data.

The Chair invited members to discuss the patient/public perspective. Members discussed the target groups identified and agreed that as the numbers were so low it was difficult to prove efficacy.

The assessment lead advised that the issue of side effects highlighted in the papers would be re-visited after the GALLIUM study is published later this year.

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

Bendamustine in combination with rituximab (MabThera®) for the treatment of previously untreated and relapsed indolent lymphomas

Date of advice: Monday 27th March 2017

Bendamustine in combination with rituximab (MabThera®) can be made available within NHS Wales for the treatment of previously untreated and relapsed follicular lymphoma, marginal zone lymphoma and Waldenstrom's macroglobulinaemia under the following circumstances:

- In the first-line setting, for use in fit patients with aggressive follicular lymphoma and marginal zone lymphoma as an alternative to rituximab plus cyclophosphamide, vincristine and prednisolone (R-CVP).

- In the relapsed setting, for use in patients with follicular lymphoma and marginal zone lymphoma where other licensed and health technology appraisal-approved regimens are unsuitable.

- For the treatment of Waldenstrom's macroglobulinaemia for first-line and relapsed disease in patients deemed unsuitable for anthracycline-based regimens and/or where other licensed and health technology appraisal-approved regimens are unsuitable.

Bendamustine in combination with rituximab is not a licensed regimen to treat this indication and is therefore 'off-label'. Each provider organisation must ensure all internal governance arrangements are completed before these medicines are prescribed in combination.

The risks and benefits of the off-label use of bendamustine with rituximab 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.

7. Date of next meeting

The Chair confirmed the next meeting would be held on Monday 24th April 2017 in Cardiff.

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