

**ALL WALES MEDICINES STRATEGY GROUP  
MINUTES OF THE AWMSG MEETING HELD ON  
WEDNESDAY, 24<sup>th</sup> JUNE 2009 COMMENCING 10.30 AM  
AT THE ANGEL HOTEL, ABERGAVENNY**

**MEMBERS PRESENT:**

**Did not  
participate in**

- |     |                       |   |            |
|-----|-----------------------|---|------------|
| 1.  | Mr Jeff Evans         | Other Professions eligible to prescribe   |            |
| 2.  | Dr Karen Fitzgerald   | National Public Health Service Wales      |            |
| 3.  | Mr Robert Holcombe    | LHB Finance Director                      |            |
| 4.  | Cllr Meurig Hughes    | Lay member                                |            |
| 5.  | Dr Thomas Lau         | General Practitioner and prescribing lead |            |
| 6.  | Mrs Susan Murphy      | LHB Pharmacist                            |            |
| 7.  | Prof Ceri Phillips    | Health Economist                          |            |
| 8.  | Mr Dave Roberts       | Chief Pharmacist                          | <b>1-7</b> |
| 9.  | Prof Philip Routledge | Clinical Pharmacologist (Chairman)        |            |
| 10. | Dr Adam Southan       | LHB Medical Director                      | <b>6-7</b> |
| 11. | Mr Guy Thompson       | Industry Representative                   |            |
| 12. | Mrs Wendy Warren      | Senior Nurse                              | <b>5-7</b> |

**IN ATTENDANCE:**

- |     |                   |                             |
|-----|-------------------|-----------------------------|
| 13. | Dr Martin Duerden | NMG Chairman                |
| 14. | Mr Russell Pope   | Welsh Assembly Government   |
| 15. | Ms Kath Haines    | Welsh Medicines Partnership |
| 16. | Mrs Ruth Lang     | Welsh Medicines Partnership |
| 17. | Mrs Karen Samuels | Welsh Medicines Partnership |

*List of Abbreviations:*

ABPI	Association of the British Pharmaceutical Industry
ASAR	AWMSG Secretariat Assessment Report
AWCDG	All Wales Cancer Drugs Group
AWMSG	All Wales Medicines Strategy Group
AWPAG	All Wales Prescribing Advisory Group
BHIVA	British HIV Association
BMA	British Medical Association
BNF	British National Formulary
CR/ASAR	Company response to the AWMSG Secretariat assessment report
CR/FAR	Company response to the final appraisal report
CR/PAR	Company response to the preliminary appraisal report
CSCG	Cancer Services Co-ordinating Group
CHM	Commission on Human Medicines
DoH	Department of Health
DTB	Drug & Therapeutics Bulletin
FAR	Final appraisal report
HCW	Health Commission Wales
HoPMMs	Heads of Pharmacy and Medicines Management
HSW	Health Solutions Wales
LHB	Local Health Board
M&TCs	Medicines & Therapeutics Committees
MHRA	Medicines & Herbs Regulatory Authority
NHSIF	NHS Industry Forum
NICE	National Institute for Health and Clinical Excellence
NLIAH	National Leadership and Innovation Agency for Healthcare
NMG	New Medicines Group
NPHS	National Public Health Service
PAR	Preliminary appraisal report
PPRS	Prescription Price Regulation Scheme
SAFF	Service and Financial Framework
SMC	Scottish Medicines Consortium
SPC	Summary of Product Characteristics
TDA User Group	Therapeutic Development Appraisal User Group
T&FG	Task and Finish Group
WAG	Welsh Assembly Government
WAPSU	Welsh Analytical Prescribing Support Unit
WeMeReC	Welsh Medicines Resource Centre
WMIC	Welsh Medicines Information Centre
WMP	Welsh Medicines Partnership

**1. Welcome and introduction**

The Chairman opened the meeting and welcomed members.

**2. Apologies**

Dr Brian Hawkins – deputy in attendance Mrs Susan Murphy  
Dr Frazer Campbell & Dr Brendon Lloyd – deputy in attendance Dr Adam Southan  
Dr Bruce Ferguson – no deputy in attendance  
Dr Paul Buss – no deputy in attendance  
Miss Carwen Wynne Howells  
Dr Geoffrey Carroll / Dr Hugo Van Woerden were not in attendance

### 3. **Declarations of interest**

The Chairman asked members to declare any specific, non-specific, personal or non-personal interests pertinent to the agenda. No interests were declared.

### 4. **Chairman's report**

The Chairman reported that following the submission of the Expert Group Review in relation to improving the availability of medicines for patients in Wales, an implementation Group, established by the Welsh Assembly Government and Chaired by Professor Roger Walker, had met on two occasions and were considering ways to take forward the recommendations of the report.

The Chairman confirmed that information in relation to the availability of medicines for the treatment of renal cell carcinoma had been submitted to Welsh Assembly government on 1<sup>st</sup> May 2009. No further information regarding this issue has been communicated via Welsh Assembly Government. The Chairman agreed to pursue this issue.

The Chairman announced that Ministerial ratification had been received for the following four positive recommendations made by AWMSG at their meeting in April.

Ambrisentan (Volibris<sup>®</sup>▼) - recommended for use within NHS Wales for the treatment of patients with pulmonary arterial hypertension (PAH) classified as World Health Organisation (WHO) functional class (FC) II and III, to improve exercise capacity.

Eculizumab (Soliris<sup>®</sup>▼) – recommended for restricted use within NHS Wales, according to agreed guidelines, for the treatment of paroxysmal nocturnal haemoglobinuria.

Maraviroc (Celsentri<sup>®</sup>▼) – recommended as an option for use within NHS Wales for the treatment of treatment-experienced adults infected only with CCR5-tropic HIV-1, in accordance with British Association (HBIVA) guidance.

Neralabine (Atriance<sup>®</sup>▼) – recommended for restricted use within NHS Wales for the treatment of patients with T-cell acute lymphoblastic leukaemia (T-ALL) and T-cell lymphoblastic lymphoma (LBL) whose disease has not responded to, or has relapsed, following treatment with at least two chemotherapy regimens. Treatment is restricted to patients in whom there is an intention to proceed to allogeneic cell transplantation, as it is not cost effective when used for palliation.

It was reported that AWMSG's advice to the Minister for Health and Social Services not to recommend the use within NHS Wales of micafungin (Mycamine<sup>®</sup>▼) for the treatment of invasive candidiasis in adults (including the elderly) and children (including neonates) will be forwarded for ratification. The applicant company challenged the interpretation of the Licence and was granted three months to seek clarification from the licensing authority. WMP representatives have held discussions with the manufacturers with regard to a potential re-submission.

The Chairman announced the appraisals to be held at the next meeting on 12<sup>th</sup> August 2009:

**Appraisal 1:** paricalcitol (Zemiplar<sup>®</sup>) for the prevention and treatment of secondary hyperparathyroidism associated with chronic renal insufficiency and chronic renal failure patients on haemodialysis or peritoneal dialysis.

**Appraisal 2:** ropinirole (Requip XL<sup>®</sup>) extended release product for the treatment of idiopathic Parkinson's Disease in patients already taking ropinirole

immediate release tablets and in whom adequate symptomatic control has been established.

**Appraisal 3:** etravirine (Intelence®) for the treatment of human immunodeficiency virus (HIV), in combination with other antiretroviral products, in treatment-experienced patients.

**Appraisal 4:** quetiapine (Seroquel XL®) for the treatment of schizophrenia

**Appraisal 5:** filgrastim (Ratiograstim®) for the treatment of neutropenia

**5. Minutes of previous meeting**

The minutes of the previous meeting were checked for accuracy. No changes were made. The Chairman signed the minutes as a true record of the previous meeting

**6. Appraisal 1 – aliskiren (Rasilez®▼)**

For the treatment of essential hypertension

Start time 10.37 am

The Chairman welcomed Danny McBryan, Marc Moodley and David Tyas representing the applicant company, Novartis Pharmaceuticals.

The Chairman confirmed that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this, and that a negative recommendation would not impact on the clinical freedom of the prescriber. He explained that a positive recommendation by AWMSG, subsequently endorsed by the Minister for Health and Social Services, places an obligation on Trusts and LHBs in Wales to fund accordingly. He reiterated that AWMSG advice is interim to NICE should it be subsequently published.

Dr Duerden set the context of the appraisal and provided an overview of the discussions held at the NMG meetings on Wednesday, 25<sup>th</sup> March 2009 and Wednesday, 20<sup>th</sup> May 2009. The relevant issues contained within the PAR, enclosure 2/AWMSG/0609, were highlighted. Members were informed that the applicant company had requested that additional information be considered, and NMG had agreed to reconsider their decision in light of this additional information. Dr Duerden confirmed that medical expert opinion was varied. NMG considered there was insufficient clinical effectiveness and health economic data to advise AWMSG that this medicine should be available within NHS Wales. The patient safety warning of the risk of angioedema and renal impairment was noted. The Chairman concluded by confirming that having taken the additional information into account NMG had reached the same conclusion and its advice to AWMSG was not to support the use of aliskiren (Rasilez®▼) for the treatment of essential hypertension within NHS Wales.

The Chairman asked members to address any outstanding issues in relation to clinical effectiveness and confirmed that opportunity would be provided to the applicant company to respond to all the issues raised in the discussion. There was discussion over the lack of direct comparisons and clinical outcome data. Members were invited to raise any issues in relation to the cost effectiveness information provided. Members noted that the model included acquisition costs, however did not account for any additional survival costs. In addition, a probabilistic sensitivity analysis was not provided.

The Chairman referred members to the patient organisation submissions from the Blood Pressure Association and the British Hypertension Society. The lay member had no additional comments. No additional societal or budget impact issues were raised.

The Chair opened the discussion to representatives of the applicant company and invited them to respond to the issues raised. There was discussion over its place in therapy, the safety data and rationale behind the selection of comparator. The unmet need of a very small group of patients was highlighted and limitations of the data accepted. The support of the British Hypertension Society was reiterated.

Prior to closing proceedings, the Chairman sought confirmation that representatives of the applicant company were satisfied that all issues had been adequately discussed and taken into account and that the process had been fair and transparent. Confirmation was received.

The Chairman closed the discussion at 11.25 am.

### **Appraisal decision**

#### **The recommendation of AWMSG was announced:**

Aliskiren (Rasilez<sup>®</sup>▼) is not recommended for use within NHS Wales for the treatment of essential hypertension. The clinical and cost effectiveness data presented was insufficient for AWMSG to recommend its use.

#### **7. Appraisal 2 – tacrolimus (Advagraf<sup>®</sup>)**

For prophylaxis of transplant rejection in adult kidney or liver allograft recipients. Treatment of allograft rejection resistant to treatment with other immunosuppressive medicinal products in adult patients

Start time 11.25 am

The Chairman welcomed Cherry Key and Manpreet Sidhu representing the applicant company, Astellas Pharma Limited.

The Chairman confirmed that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this, and that a negative recommendation would not impact on the clinical freedom of the prescriber. He explained that a positive recommendation by AWMSG, subsequently endorsed by the Minister for Health and Social Services, places an obligation on Trusts and LHBs in Wales to fund accordingly. He reiterated that AWMSG advice is interim to NICE should it be subsequently published.

Dr Duerden set the context of the appraisal and provided an overview of the discussions held at the NMG meeting on Wednesday, 20<sup>th</sup> May 2009. The relevant issues contained within the PAR, enclosure 3/AWMSG/0609, were highlighted. The Chairman relayed the concern of NMG in relation to prescribing errors reported to the MHRA. Members were informed that opinion from three medical experts had been received and all highlighted the potential for medication errors. Dr Duerden reported that NMG were not convinced that the costs were equivalent at all ranges of dosing, as the cost minimisation data provided in the submission did not prove this issue. He confirmed that NMG's advice to AWMSG was not to support the use of tacrolimus (Advagraf<sup>®</sup>▼) for prophylaxis of transplant rejection in adult kidney or liver allograft recipients. Treatment of allograft rejection resistant to treatment with other immunosuppressive medicinal products in adult patients

The Chairman invited members to address issues in relation to clinical effectiveness. There was discussion around switching and patient safety. Members explored availability of data in the rejection setting and in relation to non-Caucasians.

The Chairman referred members to the submission from the Welsh Kidney Patient Association which supported the use of tacrolimus, but did not reflect the distinction between Advagraf<sup>®</sup> and

Prograf®. The lay member confirmed he had no further comment.

The Chairman invited members to raise any outstanding issues in relation to the cost effectiveness information. The main concerns noted were that the cost minimisation evidence did not support any savings in cost. No account had been taken of the incidence of kidney rejection in the model. Treatment costs were not included in the cost minimisation or cost utilisation analysis. The cost utilisation analysis was flawed and the cost minimisation analysis did not demonstrate any savings.

It was noted that any current shared care arrangements should be reviewed to ensure hospital only prescribing. Members agreed the need to communicate the message that the product should be prescribed by brand not generically. Members expressed concern over the safety issues.

The Chairman invited members to comment on any societal or budget impact issues and then opened the discussion to representatives of Astellas. In their response the applicant company recommended prescribing by brand and confirmed their commitment to training. It was noted that changes to the packaging and SPC to highlight to healthcare professionals the dangers of unsupervised switching had been made.

Prior to closing proceedings, the Chairman sought confirmation that representatives of the applicant company were satisfied that all issues had been adequately discussed and taken into account and that the process had been fair and transparent. Confirmation was received.

The Chairman closed the discussion at 11.58 am.

#### **The recommendation of AWMSG was announced:**

Tacrolimus prolonged-release (Advagraf®) is not recommended for use within NHS Wales for the prophylaxis of transplant rejection in adult kidney or liver allograft recipients and the treatment of allograft rejection resistant to treatment with other immunosuppressive medicinal products in adult patients. The cost effectiveness data presented was insufficient for AWMSG to recommend its use.

Healthcare professionals should not stop prescribing Advagraf® for patients who are already taking it at the time of issue of this advice.

#### **8. Appraisal 3 – aripiprazole (Abilify®)**

For the treatment of moderate to severe manic episodes in Bipolar I Disorder and for the prevention of a new manic episode in certain patients.

Start time 12.25 pm

The Chairman reminded members to declare any interests.

The Chairman welcomed Toby Godsen, Emma Dudley and Martin Treur representing Bristol Myers Squibb.

The Chairman confirmed that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this, and that a negative recommendation would not impact on the clinical freedom of the prescriber. He explained that a positive recommendation by AWMSG, subsequently endorsed by the Minister for Health and Social Services, places an obligation on Trusts and LHBs in Wales to fund accordingly. He reiterated that AWMSG advice is interim to NICE should it be subsequently published.

Mr Dave Roberts joined the meeting.

Dr Duerden set the context of the appraisal and provided an overview of the discussions held at the NMG meeting on Wednesday, 20<sup>th</sup> May 2009. The relevant issues contained within the PAR, enclosure 4/AWMSG/0609, were highlighted. It was confirmed that a patient organisation submission had not been received. Dr Duerden confirmed that having taken all the information into account, including the views of the medical experts, NMG had not supported the use of this medicine as they felt the case for its cost effectiveness case had not been proven.

The Chairman opened the discussion and confirmed that opportunity would be provided to the applicant company to respond to all the issues raised.

Members were invited to address issues in relation to clinical effectiveness. There was discussion over the adverse effects of current therapy options. The metabolic profile of aripiprazole compared to other treatment options was noted. There were no outstanding issues of clinical effectiveness requiring clarification. The Chairman asked members to consider the evidence in relation to cost effectiveness. The flaws in the cost effectiveness model were highlighted by Professor Ceri Phillips. The lay member expressed disappointment at the lack of a patient organisation submission. AWMSG considered the broader societal issues including potential for limited long term treatment options and need for patient choice. Budget impact issues were noted. The Chairman invited the applicant company to respond to the issues raised in the discussion. The case for supporting the use of aripiprazole, as outlined in Bristol Myers Squibb's response to the preliminary recommendation, were highlighted.

Prior to closing proceedings, the Chairman sought confirmation that representatives of the applicant company were satisfied that all issues had been adequately discussed and taken into account and that the process had been fair and transparent. Confirmation was received.

The Chairman closed the discussion at 1.00 pm and Mrs Wendy Warren left the meeting.

### **Appraisal decision**

#### **The recommendation of AWMSG was announced:**

Aripiprazole (Abilify<sup>®</sup>) is recommended as an option for use within NHS Wales for the treatment of moderate to severe manic episodes in Bipolar I Disorder and for the prevention of a new manic episode in patients who experienced predominantly manic episodes and whose manic episodes responded to aripiprazole treatment.

#### **9. Appraisal 4 – bivalirudin (Angiox<sup>®</sup>▼)**

For the treatment of adult patients with acute coronary syndrome planned for urgent or early intervention.

The Chairman invited members to declare any interests – there were none.

The Chairman welcomed Jonathan Day and Toby Toward representing the applicant company, The Medicines Company UK Limited.

Start time 1.45 pm

The Chairman informed members that Dr Duerden had left the meeting and invited Mrs Kath Haines of the Welsh Medicines Partnership to set the context of the appraisal and provide an overview of the discussions held at the NMG meeting on Wednesday, 20<sup>th</sup> May 2009. The

relevant issues contained within the PAR, enclosure 5/AWMSG/0609, were highlighted. It was confirmed that no patient organisation submissions had been received. Three medical experts had provided opinion and members were referred to the summary of comments received. The Chairman confirmed that opportunity would be provided to the applicant company to respond to all the issues raised in discussion.

The Chairman invited members to address any outstanding issues in relation to clinical effectiveness. There was discussion over bleeding rates and the relative safety issues were noted. Professor Ceri Phillips was invited to highlight the salient issues of the cost effectiveness case. It was noted there were no utility values for acute coronary syndrome and the model excluded disutility as a result of patient bleeds. The Chairman invited comment on any outstanding issues in relation to cost effectiveness.

The lay member expressed concern that none of the patient organisations contacted provided a submission. The Chairman responded by confirming that the Expert Group Review had recommended improvement in communication with patient organisations.

The Chairman invited members to comment on any societal or budget impact issues. He then opened the discussion to representatives of the applicant company and invited a response to the issues raised. Mr Toward questioned the restriction of NMG's preliminary recommendation to a high-risk sub-group only and not all eligible patients. He highlighted the data provided which demonstrated an acceptable level of cost effectiveness to NHS Wales for both the eligible and high-risk patient groups. He drew members' attention to the salient issues in the applicant company's response to the preliminary NMG recommendation.

Prior to closing proceedings, the Chairman sought confirmation that representatives of the applicant company were satisfied that all issues had been adequately discussed and taken into account and that the process had been fair and transparent. Confirmation was received.

The Chairman closed the discussion at 2.10 pm and members retired to vote in private.

### **Appraisal decision**

#### **The recommendation of AWMSG was announced:**

Bivalirudin (Angiox<sup>®</sup>▼) (administered with aspirin and clopidogrel) is recommended as an option within NHS Wales for the treatment of adult patients with acute coronary syndromes (unstable angina/non-ST segment elevation myocardial infarction [UA/NSTEMI]) planned for urgent or early intervention.

AWMSG is of the opinion that bivalirudin (Angiox<sup>®</sup>▼) is not suitable for shared care within NHS Wales.

Bivalirudin (Angiox<sup>®</sup>▼) should only be considered as an option where both a glycoprotein IIb/IIIa inhibitor (GPI) plus heparin would be used as an alternative.

Bivalirudin (Angiox<sup>®</sup>▼) should not be used as an alternative where heparin would be used alone.

AWMSG is of the view that the main place in therapy for bivalirudin (Angiox<sup>®</sup>▼) is where there is a high risk of bleeding.

The Chairman stated that confirmation of the AWMSG recommendations in the final appraisal



reports (FARs) would be forwarded to the applicant companies within five working days. He explained that companies have up to ten days following the AWMSG meeting to accept the recommendation or lodge a request for an independent review which should be submitted in writing to the Chairman via WMP. It was confirmed that the process would not be delayed if there is a failure to respond to the deadline and, subject to receiving a request for an independent review within the appropriate timelines, the final appraisal reports would be passed to the Minister for Health and Social Services. The Chairman reported that on receipt of Ministerial ratification WMP would inform the manufacturers and post the FARs on the AWMSG website. The Chairman thanked the manufacturers for engaging with the AWMSG process and concluded appraisal proceedings

#### **10. Medication safety and health information exchange across Wales – e-prescribing**

The Chairman invited Mr Don Hughes, Director of Pharmacy in North Wales NHS Trust, to present Enc 6/AWMSG/0609 entitled 'Medication Safety and Health Information Exchange across Wales'. Mr Hughes provided the background and explained the paper provided a strong evidence base for the strategic direction for medicines management within the newly merged organisation. The report focussed on modernisation and the introduction of clinically designed information systems for medicines within and between the healthcare settings. He sought endorsement from AWMSG and other professional groups to support the case for clinically designed systems to be consistently applied across the re-organised NHS Wales.

The Chairman opened the discussion. Members agreed the need for all-party consensus to support and improve medicines management and reduce medication errors. It was suggested that an exercise be undertaken to quantify expenditure on medication errors to substantiate the case for funding, and Professor Ceri Phillips agreed to assist with the health economic quantification of savings to demonstrate the project's cost effectiveness. The Chairman agreed to convey AWMSG's unanimous support and raise the issue with the Deputy Chief Medical Officer. The Welsh Assembly Government representative suggested that it be included in the Pharmacy initiative projects. The link between prescribing and diagnosis to enable planning and collect meaningful data was welcomed. The Chairman concluded the discussion by confirming the endorsement of AWMSG and support of the project.

#### **11. Update on AWPAG**

The Chairman invited Dr Tessa Lewis to highlight the salient issues within the draft minutes of the AWPAG meeting held on 28<sup>th</sup> April 2009, Enc 8/AWMSG/0609. It was confirmed that the consultation period in relation to the update of the antiplatelet template had been extended. The paper will be presented to AWMSG at their meeting in August 2009. Dr Fitzgerald confirmed that the Antimicrobial Resistance Group is Chaired by Dr Butler. Mr Roberts confirmed a meeting he had held with representatives of Welsh Assembly Government, Community Pharmacy Wales, Boots Pharmaceuticals and Dr Brian Hawkins (AWMSG member) to discuss the issue of Special Formulations. Mr Roberts suggested a need for a high level approach to resolve the issue of specials and agreed to make contact with Mr Jonathan Simms, AWPAG Lead, to take this issue forward as a matter of urgency. It was confirmed that representatives from NHSIF would have opportunity to comment on the National Indicator 2010-2011 before it is presented to AWMSG in August.

The Chairman thanked members of the All Wales Prescribing Advisory Group for their commitment in developing the AWMSG work programme and closed the meeting.

**Date of next AWMSG meeting:**

**Wednesday, 12<sup>th</sup> August 2009 at 10.30am at The Angel Hotel, Abergavenny**