

**ALL WALES MEDICINES STRATEGY GROUP
MINUTES OF THE AWMSG MEETING HELD ON
WEDNESDAY, 25th FEBRUARY 2009 COMMENCING 10.30 AM
AT THE SWALEC STADIUM, SOPHIA GARDENS, CARDIFF**

| MEMBERS PRESENT: | | | Did not participate in |
|-------------------------|-----------------------|---|-----------------------------------|
| 1. | Dr Paul Buss | NHS Consultant (Vice Chairman) | |
| 2. | Dr Geoffrey Carroll | National Public Health Service | 9-11 |
| 3. | Dr Fraser Campbell | LHB Medical Director | |
| 4. | Mr Jeff Evans | Other professionals eligible to prescribe | |
| 5. | Dr Karen Fitzgerald | National Public Health Service Wales | |
| 6. | Dr Brian Hawkins | LHB Pharmacist | |
| 7. | Mr Robert Holcombe | LHB Finance Director | |
| 8. | Cllr Meurig Hughes | Lay member | |
| 9. | Dr Thomas Lau | General Practitioner and prescribing lead | |
| 10. | Prof Ceri Phillips | Health Economist | 6 |
| 11. | Mr Dave Roberts | Chief Pharmacist | |
| 12. | Prof Philip Routledge | Clinical Pharmacologist (Chairman) | |
| 13. | Mr Guy Thompson | Industry Representative | 8 |
| 14. | Mrs Wendy Warren | Senior Nurse | 1-5 |

IN ATTENDANCE:

| | | |
|-----|-------------------|-----------------------------|
| 14. | Dr Martin Duerden | NMG Chairman |
| 15. | Mr Russell Pope | Welsh Assembly Government |
| 16. | Ms Kath Haines | Welsh Medicines Partnership |
| 17. | Mrs Karen Samuels | Welsh Medicines Partnership |
| 18. | Mrs Ruth Lang | Welsh Medicines Partnership |

List of Abbreviations:

| | |
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| 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

Miss Carwen Wynne-Howells, Welsh Assembly Government

3. Declarations of interest

The Chairman asked members to declare any specific, non-specific, personal or non-personal interests:

Professor Ceri Phillips declared a personal specific interest in thalidomide (Thalidomide Pharmion®)

Mr Guy Thompson declared a personal non-specific interest in micafungin (Mycamine®)

The Chairman confirmed that Professor Phillips and Mr Thompson would not participate in the appraisals for which they were conflicted.

4. Chairman's report

The Chairman confirmed that the report of the Expert Group Review in relation to improving the availability of medicines for patients in Wales had been submitted to the Minister. He thanked all contributors and agreed to update members on any feedback received.

The Chairman alluded to the Minister's recent decision to allow patients in Wales greater access to four medicines used in renal cell cancer. LHBs had been instructed to provide these in appropriate patients (for sunitinib patients in the 'first line intermediate prognosis' category). The Chairman clarified the proviso that each request for funding should be supported by two cancer specialists and was a temporary arrangement until NICE made their final decision in relation to bevacizumab (Avastin®), sorafenib (Nexavar®) sunitinib (Sutent®) and temsirolimus (Torisel®) for the treatment of renal cell carcinoma. The Chairman confirmed that the AWMSG network is currently working with the cancer network in clarifying the term 'appropriate patients'.

Members were informed that NICE had issued supplementary advice to their Appraisal Committees to be taken into account when appraising treatments which may be life-extending for patients with short life expectancy, and which are licensed for indications affecting small numbers of patients with incurable illnesses. It was noted that this additional advice would apply when such treatments have an incremental cost effectiveness ratio (ICER) in excess of the upper end of the range normally approved by the Appraisal Committees and which may offer demonstrable survival benefits over current NHS practice. The Chairman confirmed that the AWMSG Steering Committee agreed that this advice should be adopted by AWMSG with immediate effect.

Dr Tom Lau joined the meeting.

The Chairman reported that following discussions at AWMSG in December the implications of withdrawing funding for the Welsh Analytical Prescribing Support Unit had been provided to the Minister.

The Chairman reported that the TDA Users Group had met on 12th January to address issues relating to the appraisal process. In addition, the three sub-groups, AWPAG, NHSIF and NMG had also met in January 2009.

The Chairman announced an Independent Review (IR) would be held on Thursday, 19th March 2009 to consider the AWMSG recommendation in relation to ambrisentan (Volibris®) for pulmonary arterial hypertension. Members were informed that the report of the IR panel would be presented to AWMSG at their meeting in April.

The Chairman confirmed that Ministerial endorsement had been received in relation to the following AWMSG recommendations:

Alemtuzumab (MabCampath®▼)

was recommended for restricted use within NHS Wales for the treatment of patients with B-cell chronic lymphocytic leukaemia (B-CLL) for whom fludarabine combination

chemotherapy is not appropriate. Alemtuzumab (MabCampath®▼) was restricted for use in patients with previously untreated B-CLL with the cytogenetic abnormality 17p-deletion. AWMSG advised that Alemtuzumab (MabCampath®▼) is not suitable for shared care within NHS Wales.

Atazanavir (Reyataz®▼)

was recommended as an option for use within NHS Wales for the treatment of HIV-1 infected adults in combination with other antiretroviral medicinal products: for treatment-experienced patients, in accordance with British HIV-1 Association (BHIVA) guidance. AWMSG advised that Atazanavir (Reyataz®▼) is not suitable for shared care within NHS Wales.

Atazanavir (Reyataz®▼)

was recommended as an option for use within NHS Wales for the treatment of HIV-1 infected adults in combination with other antiretroviral medicinal products: for treatment-naïve patients, in accordance with British HIV-1 Association (BHIVA) guidance. AWMSG advised that Atazanavir (Reyataz®▼) is not suitable for shared care within NHS Wales.

Members were informed that the Service had been informed and the final appraisal reports had been posted on the AWMSG website along with confirmation of receipt of Ministerial ratification.

The Chairman announced the appraisals to be held at the next AWMSG meeting on Wednesday, 29th April 2009:

Appraisal 1:

Aliskiren (Rasilez®▼) for the treatment of essential hypertension

Appraisal 2:

Eculizumab (Soliris®▼) in the treatment of paroxysmal nocturnal haemoglobinuria

Appraisal 3:

Maraviroc (Celsentri®▼) for treatment-experienced adults infected only with CCR5-tropic HIV-1

Appraisal 4:

Anidulafungin (Ecalta®▼) for the treatment of invasive candidiasis in adult non-neutropenic patients

Appraisal 5:

Nelarabine (Atriance®▼) for the treatment of T-cell acute lymphoblastic leukaemia and T-cell lymphoblastic lymphoma

5. Minutes of previous meeting

The minutes of the previous meeting were checked for accuracy. No changes were made and there were no matters arising.

6. Appraisal 1 – thalidomide (Thalidomide pharmion®)

In combination with melphalan and prednisolone as first line treatment of patients with untreated multiple myeloma, aged ≥65 years or ineligible for high-dose chemotherapy.

Professor Ceri Phillips left the meeting and Mrs Wendy Warren took a seat at the table.

Start time 10.50 am

The Chairman welcomed Dr Michael Thompson and Mr Ali Azough from Celgene.

The Chairman reminded members to declare any interests – there were none, and invited the NMG Chairman, Dr Martin Duerden, to address the Group.

Dr Duerden set the context of the appraisal and provided an overview of the discussions held at the NMG on 27th January 2009. The relevant issues contained within the PAR, enclosure 2/AWMSG/0209, were highlighted. Dr Duerden conveyed the views of the medical expert and the two patient organisations. He concluded by confirming the NMG recommendation was to support the use of thalidomide (Thalidomide Pharmion[®]) for use within NHS Wales within its licensed indication.

The Chairman opened the discussion and invited members to address issues in relation to clinical effectiveness. Following this discussion, the Chairman invited comments in relation to cost effectiveness.

The Chairman referred members to the patient organisation submissions from Leukaemia CARE and Myeloma UK.

The Chairman invited members to comment on any societal or budget impact issues in relation to the technology. No issues were raised.

The Chairman referred members to the company response to the PAR and invited Dr Thompson and Mr Azough to respond to the clinical aspects of members' discussion, and address issues in relation to the health economics aspects, particularly the modelling and differences in trial data. Mrs Haines confirmed that the revision of wording, alluded to in the CR/PAR, would be included in the final appraisal report.

Prior to closing proceedings, 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 guidance should it be subsequently published.

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 thorough. Dr Thompson and Mr Azough provided confirmation and commended AWMSG on the appraisal process.

The Chairman closed the discussion at 11.29 am and Professor Phillips returned to the meeting.

Appraisal decision

Thalidomide (Thalidomide Pharmion^{®▼}) is recommended for use within NHS Wales in combination with melphalan and prednisone* as first line treatment of patients with untreated multiple myeloma, aged ≥ 65 years or ineligible for high dose chemotherapy.

It should only be prescribed and dispensed according to the Thalidomide Pharmion Pregnancy Prevention Programme.

AWMSG is of the opinion that Thalidomide (Thalidomide Pharmion^{®▼}) is not suitable for

shared care within NHS Wales.

** The licence and trials specify the use of prednisone. This is not available in the UK, where a direct substitution of prednisolone for prednisone is made as they are considered dose-equivalent*.*

7. Appraisal 2 – efavirenz / emtricitabine / tenofovir disoproxil (as fumarate) (Atripla®)

For the treatment of HIV-1 infection in adults

Start time 11.30 am

The Chairman welcomed Dr Cham Herath and Ms Maria Caloudis from Gilead.

The Chairman reminded members to declare any interests.

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 27th January 2009. The relevant issues contained within the PAR, enclosure 3/AWMSG/0209, were highlighted. Dr Duerden informed members that the views of four medical experts had been considered by NMG in their deliberations, a summary of which had been provided to AWMSG members. He congratulated the patient organisation, the Terrence Higgins Trust, on the high standard of their submission.

Dr Duerden concluded by confirming NMG's advice to AWMSG was to support the use of efavirenz / emtricitabine / tenofovir disoproxil (as fumarate) (Atripla®) as an option for use within NHS Wales within its licensed indication and in accordance with current BHIVA guidance.

The Chairman opened the discussion and invited members to address issues in relation to clinical effectiveness. There was discussion and the issue of bioavailability of the tenofovir component was raised.

The Chairman asked members to consider the evidence in relation to cost effectiveness and invited Professor Ceri Phillips to bring to members' attention any relevant issues. The Chairman invited any questions or comments from members.

The Chairman referred members to the comprehensive response received from the Terrence Higgins Trust. The lay member complimented the Trust on the high quality of their submission. The Chairman invited members to comment on any societal or budget impact issues.

The Chairman referred members to the company response to the PAR and invited Dr Herath to respond to the discussion and provide clarification of the issues raised both in relation to the clinical effectiveness and cost effectiveness.

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 thorough. Confirmation was received and Dr Herath thanked AWMSG.

The Chairman closed the discussion at 11.55 am.
There was a short break prior to proceeding with the next appraisal.

Appraisal decision

Efavirenz / emtricitabine / tenofovir disoproxil (as fumarate) (Atripla[®]) is recommended as an option for use within NHS Wales for the treatment of HIV-1 infection in adults with virological suppression to HIV-1 RNA levels of < 50 copies/ml on their current combination antiviral therapy for more than three months and in accordance with current BHIVA guidance.

AWMSG is of the opinion that efavirenz / emtricitabine / tenofovir disoproxil (as fumarate) (Atripla[®]) is not suitable for shared care within NHS Wales.

8. Appraisal 3 – micafungin (Mycamine[®])

For the treatment of invasive candidiasis in adults and children.

Start time 12.05 pm

Mr Guy Thompson left the meeting.
Members were reminded to confirm any declarations of interest – there were none in addition to those declared earlier.

The Chairman welcomed Dr John Northfield, Mr Warren Cook and Ms Manpreet Sidhu representing the applicant company, Astellas Pharma Limited.

Chairman reiterated the previous statement 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.

The Chairman invited Dr Duerden to provide an overview of the discussions held at the NMG. Dr Duerden set the context of the appraisal and highlighted relevant issues contained within the PAR, enclosure 4/AWMSG/0209.

Dr Duerden confirmed that NMG had considered the views of two medical experts, a summary of which had been provided to AWMSG members. It was noted that no patient organisation submission had been received - the secretariat had contacted the National Candida Society who had declined to submit.

He concluded by confirming that NMG's advice to AWMSG is that micafungin (Mycamine[®]) should not be recommended as an option for use within NHS Wales for the treatment of invasive candidiasis in adults (including the elderly) and children (including neonates). Dr Duerden stated that NMG were of the opinion that micafungin should not be considered for use within NHS Wales as the case for its cost effectiveness had not been proven. It was noted that the submission had excluded two of its licensed indications which, therefore, could not be considered.

The Chairman opened the discussion and invited members to comment or seek clarification in relation to the clinical effectiveness. Members sought clarification of the role of the agent in children and adults and the clinical scenario in relation to its use in neonates.

The Chairman asked members to consider the evidence in relation to cost effectiveness and invited Professor Ceri Phillips to bring to members' attention any relevant issues. Members sought clarification of the range of cost effectiveness issues relating to the model used, lack of QALY data and population used in the modelling.

The lay member sought clarification of the issues raised in the response by the applicant company to the preliminary appraisal report. The Chairman invited members to comment on any broader societal or budget impact issues.

The Chairman referred members to the company response to the PAR and invited Dr Northfield to comment on any issues, either within their response, or to the discussion in general.

Prior to closing proceedings, the Chairman sought confirmation that Dr Northfield was satisfied that all issues had been adequately discussed and taken into account and that the process had been fair and thorough. Confirmation was received.

The Chairman closed the discussion at 12.57 pm.

Appraisal decision

Micafungin (Mycamine^{®▼}) is not recommended for use within NHS Wales for the treatment of invasive candidiasis in adults (including the elderly) and children (including neonates).

Key factors influencing the recommendation:

The case for cost effectiveness of micafungin (Mycamine^{®▼}) has not been proven.

Additional notes:

The holder of the marketing authorisation has not made a submission to AWMSG for the appraisal of micafungin (Mycamine^{®▼}) for its other licensed indications:

- Prophylaxis of Candida infection in adults (including the elderly) and children (including neonates) undergoing allogeneic haematopoietic stem cell transplantation (SCT) or patients who are expected to have neutropenia (absolute neutrophil count < 500 cells / microL) for 10 or more days
- Treatment of oesophageal candidiasis in adults aged 16 years and over (including the elderly) for whom intravenous therapy is appropriate.

As a result, AWMSG cannot provide advice in relation to these two indications.

9. Update on NHSIF

The Chairman invited Dr Richard Greville, acting NHSIF Chairman, to update members on the work of the NHSIF. Dr Greville referred members to Enc 5/AWMSG/0209 and highlighted salient issues from the draft minutes of the January meeting. Dr Greville expressed disappointment at the NHS attendance at the October and January meetings and confirmed that this would be addressed by the AWMSG Steering Committee. Dr

Greville provided AWMSG with additional information with regard to the PPRS and, in his address, alluded to appreciation of horizon scanning forecasts in relation to affordability, the potential to improve uptake of new medicines and initiatives within the innovation package. Dr Greville commented on the increased role of NICE in relation to the complex areas of flexible pricing and assessment of the feasibility and applicability of patient access schemes. It was noted that any potential cost savings in patient access models would need to be tracked and, if appropriate, the funding transferred from DoH to WAG. The Chair invited discussion and members expressed views that the NHS reorganisation in Wales might allow opportunity for closer engagement with the industry and NHSIF might enhance development of such a relationship. The Chairman concluded by thanking Dr Greville and confirmed that opportunities for potential collaboration between the Service and Industry should continue to be developed.

10. Update on AWPAG

The Chair welcomed Dr Tessa Lewis, Chair of AWPAG, and invited her to update members on the work of AWPAG. Dr Lewis referred members to Enc 7/AWMSG/0209 and highlighted salient issues from the draft minutes of the January meeting. Dr Lewis provided further detail in relation to the work on methotrexate, special formulations, incentivising secondary care and the development of the antiplatelet template. The Chairman confirmed that AWMSG prescribing templates would be reviewed in light of new evidence or two years after publication, whichever is soonest. There was discussion over the use of Map of Medicines. Members aired their views in relation to its functionality and use as a prescribing tool. Mrs Warren offered to link with Dr Fitzgerald to address the value of the tool and potential for consideration by AWMSG. The Chairman concluded by thanking Dr Lewis and her Group for developing this aspect of the work programme of AWMSG.

11. Review of BNF Chapter 5 – Infections

The Chairman invited Karen Samuels to present Enc 8/AWMSG/0209 a document developed in the revised format by WeMeReC on behalf of WMP/WAPSU. The salient issues from the review were highlighted by Mrs Samuels and discussion ensued. Members expressed disappointment that this work could not continue due to withdrawal of funding for WAPSU as it provided valuable information to prescribers. The need for input by a health professional in interpreting the information was noted. Dr Fitzgerald updated members on the work of the Antimicrobial Resistance Group and the Chairman supported the collaborative working with AWPAG in relation to the potential development of a national indicator. The Chairman referred members to the prescribing messages within the document. Members welcomed the high-level, strategic document and wished that resources be made available to follow up important areas highlighting prescribing anomalies within NHS Wales. It was suggested that the paper be circulated widely and posted on the AWMSG website. The Chairman concluded the discussion by thanking AWPAG, WeMeReC and WMP for contributing to the development of the document.

Date of next AWMSG meeting:

Wednesday, 29th April 2009 at 10.30am in The Angel Hotel, Abergavenny