

**ALL WALES MEDICINES STRATEGY GROUP
MINUTES OF THE AWMSG MEETING HELD ON TUESDAY,
11TH DECEMBER 2007 COMMENCING 10.30 AM AT THE
ANGEL HOTEL, ABERGAVENNY, NP7 5EN**

MEMBERS PRESENT:

**Did not
participate in
agenda item**

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|-----|-----------------------|--|-----|
| 1. | Dr Phillip Banfield | NHS Consultant | |
| 2. | Dr Robert Bracchi | General Practitioner | |
| 3. | Dr Fraser Campbell | LHB Medical Director | |
| 4. | Dr Geoffrey Carroll | Health Commission Wales | |
| 5. | Mr Jeffrey Evans | Other professional eligible to prescribe | |
| 6. | Dr Bruce Ferguson | Trust Medical Director | |
| 7. | Mr Peter Harsant | Industry Representative | |
| 8. | Mr Brian Hawkins | LHB Pharmacist | |
| 9. | Cllr Meurig Hughes | Lay member | |
| 10. | Mr David Morgan | National Public Health Service Wales | |
| 11. | Prof Ceri Phillips | Health Economist | |
| 12. | Mr Dave Roberts | Chief Pharmacist | 1-7 |
| 13. | Prof Philip Routledge | Clinical Pharmacologist (Chairman) | |
| 14. | Mrs Wendy Warren | Senior Nurse | |

IN ATTENDANCE:

- | | | |
|-----|---------------------------|-----------------------------|
| 15. | Mrs Ruth Lang | Welsh Medicines Partnership |
| 16. | Mrs Carolyn Poulter | Welsh Assembly Government |
| 17. | Mrs Karen Samuels | Welsh Medicines Partnership |
| 18. | Miss Carwen Wynne-Howells | Welsh Assembly Government |

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
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
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 & Herbals Regulatory Authority
NHSIF	NHS Industry Forum
NICE	National Institute for Health and Clinical Excellence
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
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 those present.

2. Apologies

Dr Paul Buss, NHS Consultant representative

Mr Robert Holcombe, LHB Finance representative

Dr Thomas Lau, GP & Prescribing Lead representative

Mr Dave Roberts, Chief Pharmacist (unable to attend the morning session)

3. Declarations of interest

The Chairman asked members to declare any specific, non-specific, personal or non-personal interests. There were none.

4. Chairman's report

Appraisal issues:

The Chairman reported that Ministerial ratification of AWMSG recommendations in relation to the appraisals held at the October meeting had been received. The Chairman confirmed that the final appraisal reports (FARs) of the following products had been posted on the AWMSG website, the manufacturers and the Service notified.

Agalsidase alfa (Replegal®)
Idursulfase (Elaprase®)
Vinorelbine oral (Navelbine Oral®)

Appraisals for next meeting

The Chairman confirmed that the following drugs will be appraised by NMG in January and by AWMSG on Thursday 14th February 2008.

Medicine: topotecan hydrochloride (Hycamtin®) SCLC

Manufacturer: GlaxoSmithKline

Indication: Intravenous (IV) topotecan is licensed for use in patients with relapsed small cell lung cancer (SCLC) for whom re-treatment with the first-line regimen is not considered appropriate.

Medicine: topotecan hydrochloride (Hycamtin®) Cervical Cancer

Manufacturer: GlaxoSmithKline

Indication: Topotecan in combination with cisplatin for patients with carcinoma of the cervix recurrent after radiotherapy and for patients with Stage IVB disease. Patients with prior exposure to cisplatin require a sustained treatment free interval (TFI) to justify treatment with the combination.

Medicine: tacrolimus (Advagraf®)

Manufacturer: Astellas Pharma Ltd

Indication: 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.

Medicine: Tobramycin (Bramitob®)

Manufacturer: Trinity-Chiesi Pharmaceuticals

Indication: Management of chronic pulmonary infection due to *pseudomonas aeruginosa* in patients with cystic fibrosis aged 6 and older.

Medicine: epoetin delta (Dynepo®)

Manufacturer: Shire Pharmaceuticals

Indication: Treatment of anaemia in patients with chronic renal failure. Dynepo may be used in patients on dialysis and patients not on dialysis.

General issues:

Links with ABPI

Professor Routledge informed members that representatives from WMP, Dr Martin Duerden and Professor Ceri Phillips had attended the ABPI Briefing Day held on Wednesday, 21st November at the All Nations Centre to provide an update on the AWMSG appraisal process. The Chairman thanked Dr Rick Greville, Director of ABPI (Wales) for hosting the event and providing opportunity for partnership working in developing the therapeutic development appraisal process.

The Chairman confirmed that he had met with Dr David Brickwood and Dr Greville at ABPI HQ in Whitehall to discuss issues in relation to the AWMSG appraisal process and its potential broadening. Professor Routledge was pleased to report positive feedback on the current process.

BMA Conference

The Chairman informed members that he had attended and made a presentation to the BMA Conference on behalf of AWMSG, which was hosted by the Minister and held at The Angel Hotel, Cardiff on Thursday, 29th November 2007.

Meeting venue for February 2008 AWMSG meeting

The Chairman confirmed that the AWMSG meeting on 14th February 2008 meeting will be held at the Wales Millennium Stadium, as the venue at the Angel Hotel will be closed for refurbishment.

5. Minutes of previous meeting

A typographical error on page 7 was noted. Yellow Care Centre should be changed to Yellow Card Centre.

Matters arising:

There were no matters arising not on the agenda.

6. The Chairman confirmed that a request had been made to take the appraisals in reverse order. He informed members that the representatives from Bristol-Myers Squibb Pharmaceuticals Ltd (the applicant company) had confirmed they had no objections.

Appraisal 1 - Dasatanib ALL (Sprycel[®]) – Start time 11.57 am

Manufacturers: Bristol-Myers Squibb Pharmaceuticals Ltd

Indication: Adults with Philadelphia chromosome positive (PH+) ALL and lymphoid blast CML with resistance or intolerance to prior therapy.

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 & 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 confirmed the sequence of the appraisal and invited Professor Ceri Phillips to address the Group. Professor Phillips set the context of the appraisal and provided a brief overview of the discussions held at the New Medicines Group. The relevant issues contained within the PAR - Enclosure 2/AWMSG/1207 were highlighted. Professor Phillips confirmed the NMG recommendation and drew members' attention to the key factors influencing the recommendation to advise restricted use of the medicine. Professor Phillips confirmed that a Consultant Haematologist had undertaken the role of NMG lead assessor. It was noted that due to the limited data available, some non-peer reviewed data had been included in the PAR for consideration. Members were also reminded that NMG had considered the medicine within the AWMSG criteria for ultra-orphan drug status.

The Chairman opened the discussion and asked members to consider the evidence in relation to the clinical effectiveness of the new medicine within its licensed indication. Mrs Samuels informed members that the summary of medical expert's views had not been included in the PAR, but had been supplied separately to the manufacturers, AWMSG members and posted on the AWMSG website prior to the AWMSG meeting. Mrs Samuels confirmed that NMG members had full sight of the medical expert summaries and the addendum would be included in the FAR.

The Chairman confirmed that representatives from the applicant company would have opportunity to comment on issues raised by members in their discussion.

The Chairman asked members to consider the evidence in relation to the cost effectiveness and to raise any societal or budget impact issues. Members noted concern over the adverse event profile.

The Chairman invited comment on the broader societal issues and drew members' attention to the patient interest group submission received from Leukaemia Care.

The Chairman asked members to consider the issues raised in the CR/PAR, and invited representatives of the applicant company to comment on general and specific issues. Dr Ranasinghe addressed the group and provided background and clarification in relation to some of the issues raised in the general discussion.

Following the discussion, and prior to closing proceedings, Dr Ranasinghe and Ms Minda provided confirmation to the Chairman that they were satisfied that all issues had been adequately discussed and taken into account.

In the light of the discussions the Chairman asked members to make note of their initial recommendation on their aide-memoire for reference at a later stage.

The Chairman closed proceedings at 12.20 pm and confirmed that the Committee would retire at the end of the appraisal session to vote in private.

7. **Appraisal 2 - Dasatanib CML (Sprycel®) – Start time 10.55 am**
Manufacturer - Bristol-Myers Squibb Pharmaceuticals Ltd
Indication - Adults with chronic accelerated or blast phase chronic myeloid leukaemia (CML) with resistance or intolerance to prior therapy including imatinib mesilate.

The Chairman welcomed the representatives from the applicant company, Bristol-Myers Squibb:

Ms Karolina Minda – Outcomes Research
Martin Whitehead – Outcomes Research
Dr Neil Ransasinghe – Medical Science Manager

The Chairman confirmed that opportunity would be given to the above individuals to comment on the appraisal and raise issues.

Mrs Kath Haines, WMP Senior Appraisal Pharmacist, joined members at the table.

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 & 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 confirmed the sequence of the appraisal and, in the absence of Dr Martin Duerden, invited Professor Ceri Phillips, in his capacity as NMG Vice Chairman, to address the Group.

Professor Phillips set the context of the appraisal and provided a brief overview of the discussions held at the New Medicines Group. The relevant issues contained within the PAR - Enclosure 3/AWMSG/1207 were highlighted. Professor Phillips confirmed the NMG recommendation and drew members' attention to the key factors influencing the decision.

The Chairman asked members to consider any outstanding issues in relation to the clinical effectiveness. Mrs Kath Haines was invited to join the discussion. Professor Phillips confirmed that the NMG had taken into account the adverse effect profile and the potential cost of treatment of the adverse events.

The Chairman asked members to consider any outstanding issues in relation to the cost effectiveness. Professor Phillips outlined the background of the cost saving figure and defined the term 'willingness to pay'.

The Chairman invited comment on the broader society issues and, in particular, the patient interest group submission received from Leukaemia Care. It was noted there was no information presented from the patient carer perspective or from patients who are currently being treated in relation to the treatment and adverse events.

The Chairman drew members' attention to the issues raised in the CR/PAR and invited members to comment on the issues raised. Professor Phillips confirmed that NMG had considered the medicine in relation to the AWMSG criteria for ultra orphan drug status.

The Chairman asked representatives of the applicant company to comment on the general and specific issues.

Dr Rangasinghe confirmed that additional data will be available in the near future.

Prior to closing proceedings, the Chairman invited the representatives from Bristol-Myers Squibb to confirm they were satisfied that all issues had been adequately discussed and taken into account. Confirmation was received.

In the light of the discussions the Chairman asked members to make note of their initial recommendation on their aide-memoire for reference at a later stage.

The Chairman closed proceedings at 11.55 am and confirmed that the Committee would retire at the end of the appraisal session to vote in private.

Appraisal decisions

At 1.00 pm the Chairman announced the decision of AWMSG.

The Chairman reiterated 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 & Social Services, places an obligation on Trusts and LHBs in Wales to fund

accordingly. He confirmed that AWMSG advice is interim to NICE should it be subsequently published.

The recommendation of AWMSG is:

Dasatinib (Sprycel[®]) is not recommended for use within NHS Wales for the treatment of adults with Philadelphia chromosome positive (Ph+) acute lymphoblastic leukaemia (ALL) and lymphoid blast chronic myeloid leukaemia (LB-CML) with resistance or intolerance to prior therapy.

Key factors influencing the recommendation:

Based on the available evidence, AWMSG consider that dasatinib does not represent a cost-effective use of healthcare resources for the lymphoid blast phase of CML and Ph+ ALL. The economic model submitted relies on a number of substantial assumptions e.g. utility values, disease progression, which are inadequately justified. As a result an economic case was not demonstrated in patients who are resistant to usual doses of imatinib.

For patients in the blast phase of CML where imatinib is failing, AWMSG suggest that these patients should be considered for entry into clinical trials to clarify the position of further therapy.

There are no published randomised controlled trials directly comparing dasatinib with current therapeutic treatment options for patients with Ph+ ALL and LB-CML.

The recommendation of the AWMSG is:

Dasatinib (Sprycel[®]) is recommended for restricted use within NHS Wales for the treatment of adults with chronic phase chronic myeloid leukaemia (CML) and accelerated phase CML where there is resistance or intolerance to prior therapy including imatinib mesilate. The use of dasatinib for blast phase is not recommended.

Resistance to imatinib is defined in accordance with the European LeukaemiaNet criteria and on completion of mutation analysis.

Intolerance is defined as a patient experiencing prior grade 3/4 toxicity, in accordance with the National Cancer Institute Common Toxicity Criteria, to imatinib despite receiving the lowest clinically effective dose.

Dasatinib (Sprycel[®]) should only be initiated by specialists experienced in the treatment of chronic myeloid leukaemia.

Dasatinib (Sprycel[®]) is not presently recommended for shared care.

Key factors influencing the recommendation:

There are no published randomised controlled trials directly comparing dasatinib with other current therapeutic treatment options for patients with CML.

The economic case for the use of dasatinib has not been clearly demonstrated in patients with blast phase CML.

Additional note:

For blast phase disease in CML, AWMSG suggest patients should be considered for entry into clinical trials to clarify the position of further therapy.

8. AWMSG revised Constitution

The Chairman invited Mrs Poulter to address the Group. Mrs Poulter confirmed that the Constitution of AWMSG had recently been amended and endorsed by the Minister for Health & Social Services. Changes to membership included a Health Commission Wales representative and a NHS Trust Finance Director. It was noted that future appointments will be made by the AWMSG Steering Committee and approved by the Welsh Assembly Government. Chairs of the sub-groups may also attend AWMSG meetings as a non-voting member. Mrs Poulter confirmed that the appointment of Professor Philip Routledge as substantive Chairman had been endorsed by the Minister and will be reviewed in September 2008. Mrs Poulter thanked Professor Routledge for undertaking the role of acting Chairman during the interim. The Chairman proposed, and it was agreed, that the appointment of a Vice Chairman will be addressed at the next AWMSG meeting in February 2008. There was a suggestion that representation be sought from GPC Wales and Community Pharmacy Wales, and Mr Harsant asked whether the term 'for Wales' could be excluded in relation to the ABPI representative. Mrs Samuels asked members to note there is representation from GPC Wales on NHSIF and AWPAG. The Chairman confirmed there will be an opportunity to amend the Constitution in light of any future broadening of the appraisal process or at the review of AWMSG in September 2008.

Action – WMP to post updated document on AWMSG website

9. Prescribing Strategy – draft document for comment

The Chairman invited Mrs Samuels to provide an update on the prescribing strategy document. Members were informed that Enc 5/AWMSG/1207 had been presented to the NHSIF and AWPAG at their meetings in October. WMP had been tasked with editing the document to ensure that the objectives are measurable. NHSIF had highlighted the repetition between the strategic document and the appendices and there was discussion around whether the duplication should be removed, or whether the tactical appendices should be stand-alone documents. Mrs Samuels confirmed that one final brainstorming session has been arranged for Monday, 7th January 2008 and all members of NHSIF, AWPAG and AWMSG are invited to attend, or provide written comment for consideration, before the final document is brought back to AWMSG in February 2008. The intention is to allow opportunity for members to bring their views, and the views of the groups they represent, to the forum so that there is support and buy-in from the wider service.

The Chairman invited comment. Members agreed that the document should be succinct, easy to read and visionary. Members suggested that the appendices should be considerably reduced in size. The objectives are to be made clear measurable and an executive summary should be included. Members tasked WMP with further editing the document to remove duplication so that a more succinct document could be considered at the brainstorming session. Members agreed that the brainstorming session should deliver a prioritisation, action and implementation plan.

The Chairman reiterated the importance of ensuring that views are sought from members' professional colleagues.

The Chairman thanked members for their constructive comments and closed the discussion.

10. Report on NHSIF

The Chairman invited Mr Morgan, NHSIF Chairman, to address the Group. Mr Morgan drew members' attention to the salient issues from the draft minutes of the October 2007 meeting. Mrs Lang confirmed that Mr Robin Burfield of Health Solutions Wales had agreed to attend a future AWMSG meeting to update on the Medusa project. Mr Morgan asked WMP to invite Mr Burfield to a future NHSIF meeting.

The Chairman confirmed that he had received feedback from Mrs Houghton who had taken the issues raised at the AWMSG meeting held in October to the MHRA. Mrs Houghton had reported that MHRA could not confirm whether patient reporting information details could be added to the Summary of Product Characteristics. Also, MHRA had clarified that there is no legal obligation for manufacturers to include information on patient reporting in the product information leaflets. Mrs Houghton was able to establish that there are plans for a patient reporting campaign launched by the MHRA. The Chairman apologised for not raising this issue under matters arising.

Action – WMP to invite Mr Burfield to a future NHSIF meeting

11. Report on AWPAG

Dr Tessa Lewis, AWPAG Vice-Chair, joined members around the table. Dr Lewis invited comment in relation to the draft minutes of the AWPAG meeting dated October 2007. The Chairman asked Dr Lewis to update members in relation to the template for shared care of amiodarone. Dr Lewis confirmed that this is now being discussed at local level. Professor Routledge confirmed he had received positive comments in relation to the template. It was noted that the timescale for development of the prescribing indicators had been omitted from the draft minutes. A suggestion was made that AWPAG should consider updating the statin template in light of guidance issued by NICE in November 2007. Dr Lewis agreed to take the comments received back to AWPAG in January 2008.

Action – WMP to insert timescale for prescribing indicators into the draft minutes

12. Summary of feedback regarding the broadened appraisal process

The Chairman invited Mrs Samuels to present Enc 8/AWMSG/1207. Members were informed that WMP had circulated questionnaires and received feedback from members of AWMSG, NMG and WMP. In addition, WMP had met with the TDA Users Group and representatives of applicant companies who had experienced the first two cycles of the broadened appraisal process to gather information and feedback. Mrs Samuels informed members that Enc 8/AWMSG/07 provided general comment on the process and confirmed that WMP had implemented changes in light of the comments received. It was confirmed that an AWMSG/NMG Training Day in Health Economics had been arranged on Friday, 8th February 2008 at Cardiff Rugby Football Club at which key representatives of MTCs and the Cardiac/Cancer Networks had also been invited. The Chairman confirmed that WMP carefully considers costs, accessibility for members from all parts of Wales, visitors and technical support, and quality of service provided, in deciding upon meeting venues. Members agreed that provided the costs of the Abergavenny venue remained favourable compared with alternative venues, meetings should continue to be held at its present location.

Date of next AWMSG meeting: Thursday, 14th February 2008 at the Wales Millennium Stadium commencing 10.30 am.