

Enclosure No:	1/AWMSG/0611
Agenda Item No:	5 – Minutes of previous meeting
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ALL WALES MEDICINES STRATEGY GROUP

MINUTES OF THE AWMSG MEETING HELD ON WEDNESDAY, 13th APRIL 2011 COMMENCING 10.30 AM AT THE ANGEL HOTEL, ABERGAVENNY

MEMBERS PRESENT:

**Did not
participate in**

- | | | | |
|-----|-----------------------|------------------------------------------------------|------------|
| 1. | Dr Bruce Ferguson | Medical Director & Acting Chairman | |
| 2. | Dr Balwinder Bajaj | Clinical Pharmacologist | |
| 3. | Dr Philip Banfield | Hospital Consultant | |
| 4. | Dr Fraser Campbell | General Practitioner | |
| 5. | Prof David Cohen | Health Economist | |
| 6. | Mrs Debbie Davies | Representing other professions eligible to prescribe | |
| 7. | Mr Stefan Fec | Community Pharmacist | |
| 8. | Dr Karen Fitzgerald | Consultant in Pharmaceutical Public Health | |
| 9. | Dr Brian Hawkins | Senior Primary Care Pharmacist | |
| 10. | Mr Christopher Palmer | Lay member | |
| 11. | Mrs Rebecca Richards | Finance Director | |
| 12. | Mr Guy Thompson | ABPI (Wales) representative | |
| 13. | Dr Hugo van Woerden | Welsh Health Specialised Services Committee | |
| 14. | Mrs Wendy Warren | Senior Nurse | |
| 15. | Dr John Watkins | Consultant in Public Health Medicine | 1-5 |

IN ATTENDANCE:

- | | | |
|-----|-------------------------|---------------------------------|
| 16. | Dr Robert Bracchi | Chairman, New Medicines Group |
| 17. | Professor Ceri Phillips | NMG/AWMSG Link Health Economist |
| 18. | Mr Roger Walker | Welsh Assembly Government |
| 19. | Mrs Karen Samuels | Welsh Medicines Partnership |
| 20. | Ms Kath Haines | Welsh Medicines Partnership |
| 21. | Mrs Ruth Lang | Welsh Medicines Partnership |

List of Abbreviations:

ABPI	Association of the British Pharmaceutical Industry
ASAR	AWMSG Secretariat Assessment Report
AWMSG	All Wales Medicines Strategy Group
AWPAG	All Wales Prescribing Advisory Group
DH	Department of Health
EMA	European Medicines Agency
FAR	Final Appraisal Recommendation
GP	General Practitioner
HAC	High Acquisition Cost
HB	Health Boards
M&TCs	Medicines & Therapeutics Committees
NICE	National Institute for Health and Clinical Excellence
NMG	New Medicines Group
NPHS	National Public Health Service
PAR	Preliminary Appraisal Recommendation
SMC	Scottish Medicines Consortium
TDA Partnership Group	Therapeutic Development Appraisal Partnership Group
T&FG	Task and Finish Group
WAG	Welsh Assembly Government
WAPSU	Welsh Analytical Prescribing Support Unit
WMP	Welsh Medicines Partnership

1. Welcome and introduction

The Chairman opened the meeting and welcomed members.

2. Apologies

Professor Philip Routledge, AWMSG Chairman (Dr Bruce Ferguson deputising)
Dr Emma Mason, Clinical Pharmacologist (Dr Balwinder Bajaj deputising)
Mr Roger Williams & Mr John Terry (representing senior hospital pharmacists)

3. Declarations of interest

The Chairman asked members to declare any interests pertinent to the agenda. There were none.

4. Chairman's report

The Chairman announced that the Minister for Health and Social Services had ratified the following AWMSG recommendations from the February meeting. He confirmed the Service had been informed and the final appraisal reports posted on the AWMSG website.

Filgrastim (Nivestim[®]▼) is recommended as an option for use within NHS Wales for the treatment of neutropenia:

- For the reduction in the duration of neutropenia and the incidence of febrile neutropenia in patients treated with established cytotoxic chemotherapy for malignancy (with the exception of chronic myeloid leukaemia and myelodysplastic syndromes) and for the reduction in the duration of neutropenia in patients undergoing myeloablative therapy followed by bone marrow transplantation considered to be at increased risk of prolonged severe neutropenia. The safety and efficacy of filgrastim are similar in adults and children receiving cytotoxic chemotherapy.

- For the mobilisation of peripheral blood progenitor cells (PBPC).

- In patients, children or adults, with severe congenital, cyclic, or idiopathic neutropenia with an absolute neutrophil count (ANC) of $0.5 \times 10^9/l$ and a history of severe or recurrent infections, long term administration of (Nivestim[®]▼) is indicated to increase neutrophil counts and to reduce

the incidence and duration of infection-related events.

- For the treatment of persistent neutropenia (ANC less than or equal to $0.5 \times 10^9/l$) in patients with advanced HIV infection, in order to reduce the risk of bacterial infections when other options to manage neutropenia are inappropriate.

- Filgrastim (Nivestim[®]▼) is not suitable for shared care within NHS Wales for the above indication.

- Filgrastim (Nivestim[®]▼) should be prescribed by brand name to avoid automatic substitution and therefore help with pharmacovigilance.

Valsartan (Diovan[®]▼) tablets are not recommended for use within NHS Wales for the treatment of hypertension in children and adolescents 6 to 18 years of age.

The submission contained insufficient evidence for AWMSG to recommend its use.

Darunavir (Prezista[®]▼) co-administered with low dose ritonavir, in combination with other antiretroviral medicinal products, is recommended as an option for use within NHS Wales for the treatment of human immunodeficiency virus (HIV-1) infection in antiretroviral treatment (ART)-experienced children and adolescents from the age of 6 years and at least 20 kg body weight. Darunavir (Prezista[®]▼) should be prescribed in accordance with Paediatric European Network for Treatment of Aids (PENTA) guidelines.

Darunavir (Prezista[®]▼) is not suitable for shared care within NHS Wales for the above indication

The Chairman confirmed that since the last AWMSG meeting and, in the absence of a submission from the holder of the marketing authorisation, one statement of advice had been issued. It was announced that paliperidone (Invega[®]) cannot be endorsed for use within NHS Wales for the treatment of psychotic or manic symptoms of schizoaffective disorder. The Chairman reiterated that this medicine should not be routinely available within NHS Wales.

Members were informed that on 7th April 2011 representatives from AWMSG and WMP attended the launch of the updated ABPI Code of Practice for the Pharmaceutical Industry. The Chairman informed members that the Code is the main means by which the promotion of prescription medicines is regulated in the UK and it reflects and extends beyond UK law. Members were provided with a copy of the Code for information.

It was announced that no appraisals had been scheduled for the next AWMSG meeting in May. At the AWMG Steering Committee held in April, it was agreed that a Training Day for AWMSG and NMG members and deputies would be held on 18th May. The Chairman announced the next AWMSG meeting would be held on 15th June and the following appraisals would be undertaken:

Valganciclovir (Valcyte[®]) (tablets): licence extension for 200 days prophylaxis of cytomegalovirus (CMV) disease in CMV-negative kidney transplant patients who have received a transplant from a CMV-positive donor

Valganciclovir (Valcyte[®]) (powder for oral solution): licence extension for 200 days prophylaxis of cytomegalovirus (CMV) disease in CMV-negative kidney transplant patients who have received a transplant from a CMV-positive donor

Applicant company - Roche Products Ltd

Tacrolimus (Advagraf[®]) for the 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.

5. Minutes of previous meeting

The minutes of the previous meeting were checked for accuracy. Mr Guy Thompson raised an issue of accuracy under agenda item 12 and members agreed a correction to the wording should be made. AWMSG members had requested clarification of the AWPAG minutes on the item under any other business relating to the recent 'MHRA warning' on dronedarone, not 'withdrawal' of dronedarone as stated in the minutes. It was noted that the correction should also state "She concluded by informing members that the update of the template for prescribing lipid lowering agents would be included on the agenda at a future meeting". Dr Philip Banfield asked that the minutes be amended to reflect that he had brought the 1000 Lives Campaign Transforming Maternity Care mini-collaborative to the attention of the committee since he is the Faculty Lead for this initiative. He had highlighted that the mini-collaborative was focusing on venous thromboembolism prevention and the management of the acutely deteriorating woman in pregnancy, with a specific focus on sepsis. This links in with the work on low molecular weight heparin prescribing in Wales brought to AWMSG by WMP previously, because it aims to resolve the issues highlighted regarding the lack of obstetric consensus guidelines in Wales. AWMSG was supportive of the collaborative work. Mrs Rebecca Richards highlighted that she had been recorded as 'in attendance' and it was confirmed that she had not attended the previous meeting.

With these amendments, the Chairman signed the minutes as a true record of the previous meeting. There were no matters arising.

6. Appraisal 1 - histamine dihydrochloride (Ceplene®▼) maintenance therapy for adult patients with acute myeloid leukaemia in first remission concomitantly treated with interleukin-2

The Chairman invited members to declare interests in either the applicant company or the medicine. There were none. The Chairman welcomed the delegates from the applicant company, Meda Pharmaceuticals.

The Chairman announced the statement, pertinent to all appraisals, that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this. A negative recommendation would not impact on the clinical freedom of the prescriber. It was noted that a positive recommendation by AWMSG, subsequently endorsed by the Minister for Health and Social Services, places an obligation on Health Boards to fund accordingly. It was confirmed that AWMSG advice is interim to final NICE guidance should this be subsequently published.

The Chairman reiterated that NMG had considered the clinical and cost effectiveness issues in detail and had taken account of medical expert and patient organisation views. Members were reminded not to repeat the detailed discussion held at NMG but to seek clarification of any outstanding issues in relation to clinical or cost-effectiveness, consider the company response to the preliminary recommendation and take into account societal and budget impact issues. He confirmed that members would retire to vote in private and agree the recommendation, which would be subsequently announced.

The Chairman invited Dr Robert Bracchi, Chairman of the New Medicines Group, to provide an overview of the discussions held at the preliminary appraisal. Dr Bracchi set the clinical context as outlined in the ASAR. In his address, Dr Bracchi relayed the views of clinical experts. He confirmed that no patient organisation submission had been received.

Dr Bracchi explained why NMG considered that histamine dihydrochloride (Ceplene®▼) should not be recommended for use within NHS Wales for maintenance therapy for adult patients with acute myeloid leukaemia in accordance with its licensed indication. Members were informed that NMG considered the case for clinical effectiveness and cost effectiveness had not been

proven and there were several uncertainties and limitations in the economic model provided within the company's submission. NMG suggested that further clinical studies would be necessary to substantiate its clinical effectiveness.

The Chairman opened the discussion and invited members to highlight issues in relation to the case for clinical effectiveness. Members sought clarification in relation to the positive treatment effects and adverse events. The Chairman asked the company delegates to highlight the sub-group analysis with regard to age. It was noted that the medicine was not effective in patients over the age of sixty. Dr Bracchi confirmed that NMG had appraised the whole of the licensed indication and also the under sixty age group. Dr Bracchi relayed NMG's view that the evidence submitted in the under-sixty age group had been insufficient in that it was a small group of patients.

The Chairman invited Professor Ceri Phillips to highlight issues in relation to cost effectiveness. It was acknowledged that the company response to the PAR had addressed some of the outstanding issues and was very helpful. Professor Phillips confirmed that discussions at NMG in relation to the cost effectiveness model had been discussed at length. NMG had not been convinced that the information provided was sufficient to recommend its use due to the high level of uncertainty.

It was noted the lay member had no comment. The Chairman referred members to the summary of clinical expert opinion which stated as there is no maintenance therapy currently available; histamine dihydrochloride (Ceplene[®]▼) could meet an unmet clinical need in this condition.

The company delegates responded to all the issues raised in the discussion, both clinical and in relation to their case for cost effectiveness. They provided clarification in relation to costs and changes in costs over time. It was confirmed that Meda Pharmaceuticals had no connection with interleukin-2. Clarification in relation to positive treatment effects, method of randomisation, and cost utility issues was provided. The company delegates highlighted the significant differences in incremental effect between the sub-groups and confirmed that from a clinical perspective it would be feasible to restrict the availability of the medicine.

Prior to concluding the appraisal, the Chairman asked the company delegates to confirm that all the outstanding issues had been addressed and confirmation was given by the delegates that the process had been fair and transparent.

The Chairman asked members to make a note of their comments on the aide-memoire provided. He confirmed that members would retire to vote at the end of the appraisal session and the recommendation would be subsequently announced.

Appraisal decision

AWMSG's recommendation to the Minister for Health and Social Services was announced:

Histamine dihydrochloride (Ceplene[®]▼) is not recommended for use within NHS Wales for maintenance therapy for adult patients with acute myeloid leukaemia in accordance with its licensed indication. The case for clinical effectiveness and cost effectiveness has not been proven.

7. Appraisal 2 - capecitabine (Xeloda[®]) in combination with oxaliplatin for the adjuvant

treatment of stage III (Dukes' stage C) colon cancer

The Chairman invited members to declare interests in either the applicant company or the medicine. There were none. The Chairman welcomed the delegates from the applicant company, Roche Products Limited.

The Chairman announced the statement, pertinent to all appraisals, that AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this. A negative recommendation would not impact on the clinical freedom of the prescriber. It was noted that a positive recommendation by AWMSG, subsequently endorsed by the Minister for Health and Social Services, places an obligation on Health Boards to fund accordingly. It was confirmed that AWMSG advice is interim to final NICE guidance should this be subsequently published.

The Chairman reiterated that NMG had considered the clinical and cost effectiveness issues in detail and had taken account of medical expert and patient organisation views. Members were reminded not to repeat the detailed discussion held at NMG but to seek clarification of any outstanding issues in relation to clinical or cost-effectiveness, consider the company response to the preliminary recommendation and take into account societal and budget impact issues. He confirmed that members would retire to vote in private and agree the recommendation, which would be subsequently announced.

The Chairman invited Dr Robert Bracchi to provide an overview of the discussions held at the preliminary appraisal. Dr Bracchi set the clinical context as outlined in the ASAR. He relayed the views of the clinical experts and confirmed that a patient organisation submission by Bowel Cancer UK was considered by NMG. Dr Bracchi explained the reasons why members of the New Medicines Group had concluded that capecitabine (Xeloda[®]) in combination with oxaliplatin should be recommended as an option for use within NHS Wales for the adjuvant treatment of patients following surgery of stage III (Dukes' stage C) colon cancer. NMG were of the opinion that capecitabine (Xeloda[®]) would not be suitable for shared care within NHS Wales for this indication.

The Chairman opened the discussion and invited members to highlight any issues in relation to the case for clinical effectiveness. There were no outstanding clinical issues of note and the Chairman moved on to cost effectiveness issues. There were no outstanding issues in relation to the case for cost effectiveness and the company delegates highlighted the potential drug and administration cost savings. Mr Palmer reiterated the strong support for this medicine from the patient organisation and the Chairman referred members to the summary of clinical expert opinion.

In concluding the appraisal, the Chairman confirmed that members would retire to vote and the recommendation would be subsequently announced.

Appraisal decision

AWMSG's recommendation to the Minister for Health and Social Services was announced:

Capecitabine (Xeloda[®]) in combination with oxaliplatin is recommended as an option for use within NHS Wales for the adjuvant treatment of patients following surgery of stage III (Dukes' stage C) colon cancer.

Capecitabine (Xeloda[®]) is not suitable for shared care within NHS Wales for the above indication.

8. The nature and scope of benzodiazepine and 'z' drug

prescribing in Wales – Educational pack

The Chairman invited Ms Kath Haines to present Enc 4/AWMSG/0411 - the nature and scope of benzodiazepine and 'z' drug prescribing in Wales – educational pack. Members were informed that a project had been initiated as a result of a report produced in 2008 highlighting evidence of increased prescribing of benzodiazepine and new generation 'z' drugs. As part of the new strategy to tackle substance misuse, a project was designed to look at reducing inappropriate prescribing of benzodiazepine and 'z' drugs in Wales. The study was commissioned through the Welsh Medicines Partnership (WMP) and a report was presented to AWMSG in March 2011 by Mrs Karen Eveleigh which showed an overall reduction in prescribing levels. It was noted that the level of prescribing is higher than that in the benchmarked area of North East England. Members were informed that an educational toolkit had been developed by WMP which, if available electronically, could be useful for specialists and general practitioners (GPs) in consultation with patients.

Members were informed there had been reluctance within the Assembly to develop an educational pack and issue more guidance. However, AWMSG had acknowledged the difficulty in accessing in one place specific data/guidance on benzodiazepine prescribing and advocated the development of the educational toolkit to promote best practice. AWMSG noted the toolkit template could be adapted locally to suit individual needs to ensure consistency across health boards. It was also noted that the toolkit is aimed both at primary care, community and the hospital settings. AWMSG considered the educational pack and toolkit would provide a useful tool for health boards when reviewing data at local level. It was confirmed that the Welsh Assembly Government logo would be removed from the draft document. It was suggested that alternative wording was required to clarify the section in relation to benzodiazepine prescribing in pregnancy and Dr Banfield offered to provide the appropriate wording outside of the meeting. It was noted that Table 2 on page ten should be amended to read 'gynaecology' instead of 'obstetric'. Members supported a targeted initiative within health boards with regard to the usage of benzodiazepines. It was suggested that acute issues need to be explored and recognition was expressed that a public message and promotion of messages would be required. Members agreed that patient education is crucial to ensure the success of this initiative.

There was discussion regarding the dissemination, implementation and audit of the educational toolkit, and members suggested mechanisms for this. WMP noted the need for a multi-professional approach to support the work and agreed to identify relevant professional groups to support the implementation. The Chairman closed the discussion and confirmed AWMSG's endorsement of the document as a useful support to the management and usage of benzodiazepine prescribing. He recognised the role of health boards in ensuring the appropriate use of the educational pack.

9. Review of the Limited Submission Process (Form C)

The Chairman invited Ms Kath Haines from the Welsh Medicines Partnership to present Enc 5/AWMSG/0411 a proposal that AWMSG should retain its limited submission process (Form C) with minor modifications to the paperwork and process that had recently been piloted. Ms Haines explained that as part of the broadening of AWMSG's appraisal remit in October 2010 to include all new medicines and licence extensions/formulations, a pilot of a Limited Submission process had been undertaken. In conjunction with the TDA Partnership Group, WMP had developed a process aligned to that of the Scottish Medicines Consortium's (SMC) abbreviated process. It was hoped that the limited process would encourage companies to submit for appraisal of medicines for which they may not usually engage. Five pharmaceutical companies had participated in the pilot. Following completion of six appraisals using the limited submission process, feedback had been sought from the applicant companies, members of the New Medicines group (NMG), AWMSG members and the Welsh Medicines Partnership (WMP) appraisal teams. Ms Haines explained the paper provided an overview of the feedback received and suggested considerations for the future of a limited submission process. It was suggested to AWMSG that WMP would prepare the assessment report (i.e. the ASAR)

and make a recommendation to the New Medicines Group with regard to the availability of the medicine within NHS Wales. The applicant company would have opportunity to comment on the recommendation as part of their company response to the ASAR. If the applicant company accepted the WMP recommendation, then NMG would not consider the application in detail and would normally accept the WMP advice as their preliminary recommendation to AWMSG. If the applicant company did not accept the recommendation, then NMG would consider the submission and make a preliminary recommendation to AWMSG along the same lines as the full submission.

Members were informed that an additional criterion would be included in Form C – “If the estimated difference in cost compared with the appropriate comparator is deemed by the AWMSG Steering Committee to be small”. It was noted that monitoring the budget impact would be essential, and AWMSG reserved the right to request a full submission if the budget impact exceeded that estimated in the limited submission.

The Chairman invited comment on the proposal. There was a suggestion that an amendment be made to section 4.3 in that ‘some’ should be changed to ‘sufficient’ as it was considered this wording challenged the level of data supplied in the limited submission. In closing the discussion, the Chairman confirmed that AWMSG supported the proposal of the Steering Committee.

10. AWMSG response to Department of Health Consultation on value based pricing – for information

The Chairman confirmed that a copy of AWMSG’s response to the Department of Health Consultation on value based pricing had provided to members for information.

11. Denosumab (Prolia®▼) for the prevention of osteoporotic features in postmenopausal women

The Chairman invited Dr Tessa Lewis to present Enc 7/AWMSG/0411 a proposal from AWPAG recommending the place for the prescribing in Wales of denosumab (Prolia®▼) for the prevention of osteoporotic fractures in postmenopausal women. Members were informed that AWPAG proposed that denosumab (Prolia®▼) should only be prescribed in accordance with NICE guidelines (technology appraisal 204). It was suggested that denosumab should be initiated by a specialist within secondary care for the first two doses (one year) and thereafter prescribing and administration responsibility may be transferred to primary care. AWPAG did not consider that a shared care protocol would be necessary, to allow the transfer of clinical responsibility for prescribing and administration of denosumab for this indication. Dr Lewis highlighted that denosumab is a new biological agent that affects other body systems (including the immune system), and that long-term adverse events could not be ruled out. Members were informed the document had undergone minor changes following national consultation. The Chairman opened the discussion and clarification was sought in relation to the wording of the paragraph under 3.0 Summary. Dr Lewis agreed to modify the wording of this section to provide greater clarity in relation to the prescribing and administration responsibility after twelve months. Speaking on behalf of the industry, Mr Thompson confirmed that the manufacturers had welcomed the engagement with AWPAG, but had considered there had been lack of clarity with regard to the process for engagement. Dr Lewis confirmed that the draft document had been updated in light of comments received from the manufacturer, and relayed general comments received from stakeholders during the consultation process. With the qualification of wording under 3.0 Summary, the Chairman confirmed that AWMSG endorsed the guidance developed by AWPAG.

AWMSG Training day: Wednesday, 18th May 2011

Date of next meeting: Wednesday, 15th June 2011 at The Angel Hotel, Abergavenny