Enclosure No:	**1/AWMSG/1210**
Agenda Item No:	**5** – Minutes of previous meeting
Author:	Chairman, AWMSG
Contact:	Tel: 029 20716900 E-Mail: wmp@wales.nhs.uk

ALL WALES MEDICINES STRATEGY GROUP

MINUTES OF THE AWMSG MEETING HELD ON WEDNESDAY, 13th OCTOBER 2010 COMMENCING 10.30 AM AT THE ANGEL HOTEL, ABERGAVENNY

MEMBERS PRESENT:

Did not participate in

1.	Prof Philip Routledge	Chairman
2.	Dr Paul Buss	Hospital Consultant
3.	Prof David Cohen	Health Economist
4.	Mrs Debbie Davies	Representing other professions eligible to prescribe
5.	Dr Bruce Ferguson	Medical Director
6.	Dr Karen Fitzgerald	Consultant in Pharmaceutical Public Health
7.	Dr Brian Hawkins	Senior Primary Care Pharmacist
8.	Ms Louise Hendry	ABPI (Wales) representative
9.	Cllr Meurig Hughes	Lay representative
10.	Ms Ellen Lanham	Community Pharmacist
11.	Dr Emma Mason	Clinical Pharmacologist
12.	Dr John Watkins	Consultant in Public Health Medicine
13.	Dr William Whitehead	General Practitioner
14.	Mr Roger Williams	Senior Hospital Pharmacist

IN ATTENDANCE:

15.	Dr Robert Bracchi	NMG Chairman
16.	Professor Ceri Phillips	NMG Health Economist
17.	Mr Jeremy Savage	Welsh Assembly Government
18.	Mrs Karen Samuels	Welsh Medicines Partnership
19.	Mrs Ruth Lang	Welsh Medicines Partnership
20.	Ms Kath Haines	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
IHC	Informing Healthcare
HB	Health Boards
M&TCs	Medicines & Therapeutics Committees
MHRA	Medicines & Healthcare Products Regulatory Agency
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 Geoffrey Carroll, Welsh Health Specialised Services Committee (deputy not in attendance)
Mrs Wendy Warren, Senior Nurse (deputy not in attendance)
Ms Rebecca Richards, Finance Director (deputy non in attendance)
Mr Guy Thompson, ABPI representative (deputy in attendance)

3. Declarations of interest

Louise Hendry declared a professional conflict in relation her employer Pfizer Limited and agenda item 8 – update paper on low molecular weight heparin.

4. Chairman's report

The Chairman expressed thanks to Councillor Meurig Hughes who, after completing his full term of office, had agreed to stand in as lay member and represent the patient interest.

It was reported that following receipt of the Minister's approval of the updated AWMSG Constitution, applications for new membership to AWMSG and its sub-groups had been processed. The Chairman welcomed:

Dr Emma Mason, Clinical Pharmacologist
Dr Bill Whitehead, deputising for Dr Fraser Campbell
Ms Ellen Lanham, Community Pharmacist
Professor David Cohen, Health Economist
(Professor Ceri Phillips will be the voting member at NMG and will attend AWMSG as the NMG link)
Dr John Watkins, Consultant in Public Health Medicine

It was noted that Dr Fraser Campbell had taken on the role as AWMSG GP representative and Professor Ceri Phillips would vote at NMG and attend future AWMSG meetings as a non-voting link member.

The Chairman expressed thanks to Mr Dave Roberts who has stepped down from AWMSG. Mr Roger Williams had taken up the position as AWMSG Senior Pharmacist, and Mr John Terry had been appointed as a deputy senior pharmacist representative. It was confirmed that an updated list of AWMSG and AWPAG members and deputies would be available on the AWMSG website.

The Chairman drew members' attention to the updated constitutions of the New Medicines Group and All Wales Prescribing Advisory Group. The constructive collaborative working relationship developed via the NHS Industry Forum, chaired first by Mr David Morgan and subsequently by Dr Richard Greville, was acknowledged. Members noted that this mature relationship had resulted in industry representation into the All Wales Prescribing Advisory Group.

The Chairman highlighted the major campaign launched by the Welsh Assembly on 14th September 2010 which aims to save millions of pounds by reducing the amount of wasted medicines.

The Chairman announced that the Minister for Health and Social Services had ratified the recommendations of AWMSG from the August meeting:

Epoetin alfa (Binocrit®▼) is recommended as an option for restricted use within NHS Wales in accordance with NICE Clinical Guidance 39 for the treatment of symptomatic anaemia associated with chronic renal failure in adult and paediatric patients:

- Treatment of anaemia associated with chronic renal failure in paediatric and adult patients on haemodialysis and adult patients on peritoneal dialysis

- Treatment of severe anaemia of renal origin accompanied by clinical symptoms in adult patients with renal insufficiency not yet undergoing dialysis

AWMSG is of the opinion that epoetin alfa (Binocrit®▼) is not suitable for shared care within NHS Wales.

Epoetin alfa (Binocrit®▼) should be prescribed by brand name to avoid automatic substitution and therefore help with pharmacovigilance.

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

- For 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 children and adults, with severe congenital, cyclic, or idiopathic neutropenia with an absolute neutrophil count (ANC) of ≤ 0.5 x 10^9/l and a history of severe or recurrent infections, long term administration of TevaGrastim®▼ is indicated to increase neutrophil counts and to reduce the incidence and duration of infection-related events.

- For the treatment of persistent neutropenia (ANC ≤ 1.0 x 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.

AWMSG is of the opinion that filgrastim (TevaGrastim®▼) is not suitable for shared care within NHS Wales.

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

Filgrastim (Zarzio®▼) 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 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.

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

- In children and adults with severe congenital, cyclic, or idiopathic neutropenia with an absolute neutrophil count (ANC) of ≤ 0.5 x 10^9/l, and a history of severe or recurrent infections, long term administration of filgrastim is indicated to increase neutrophil counts and to reduce the incidence and duration of infection-related events.

- For the treatment of persistent neutropenia (ANC ≤ 1.0 x 10^9/l) in patients with advanced HIV infection, in order to reduce the risk of bacterial infections when other therapeutic options are inappropriate.

AWMSG is of the opinion that filgrastim (Zarzio®▼) is not suitable for shared care within NHS Wales.

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

Members were informed that since the last AWMSG meeting and in the absence of a submission from the holder of the marketing authorisation, a statement of advice had been issued confirming that the following medicines cannot be endorsed for use and should not be routinely available within NHS Wales:

- **capecitabine (Xeloda®)** in combination with oxaliplatin based chemotherapy for the adjuvant treatment of stage III colon cancer

- **delta-9-tetrahydrocannabinol/cannabidiol (Sativex®)** as add-on treatment, for symptom improvement in patients with moderate to severe spasticity due to multiple sclerosis

- **rosuvastatin (Crestor®)** for the prevention of major cardiovascular events in patients who are estimated to have a high risk for a first cardiovascular event, as an adjunct to correction of other risk factors

- **ferric carboxymaltose (Ferinject®)** for the treatment of iron deficiency when oral iron preparations are ineffective or cannot be used

- **hydroxycarbamide (Siklos®)** for the prevention of vaso-occlusive crises in patients with symptomatic sickle cell syndrome

- **somatropin (Omnitrope®)** for replacement therapy in adults with pronounced growth hormone deficiency

The Chairman announced five appraisals scheduled for the next AWMSG meeting on 15th December. It was noted that four were limited submissions and one a re-submission. Members were informed that the limited submission process (i.e. Form C) is currently being piloted and a review of the process would subsequently be undertaken. Members were informed that the relevant documentation had been made available on the AWMSG website for information but would be subject to review.

Appraisal 1 (full submission)
Ranolazine (Ranexa®) for treatment of stable angina pectoris

Appraisal 2 (limited submission)
Sildenafil citrate (Revatio®) for treatment of patients with pulmonary arterial hypertension who are currently prescribed oral sildenafil citrate and who are temporarily unable to take oral medicine

Appraisal 3 (limited submission)
Atazanavir (Reyataz®) for the treatment of HIV-1 infected paediatric patients in combination with other antiretroviral medicinal products

Appraisal 4 (limited submission)
Tipranavir (Aptivus®) for treatment of HIV-1 infection in highly pre-treated adolescents 12 years of age or older with no other therapeutic options

Appraisal 5 (limited submission)
Tipranavir (Aptivus®) for treatment of HIV-1 infection in highly pre-treated children from 2 to 12 years of age with no other therapeutic options

The Chairman confirmed that AWMSG's recommendation in relation to **Cetuximab (Erbitux®▼)** for third-line treatment of patients with KRAS wild-type metastatic colorectal cancer would shortly be forwarded to Welsh Assembly for ministerial ratification. The applicant company, Merck Serono Ltd, had raised issues in relation to AWMSG's interpretation of NICE's advice for appraising end of life medicines.

5. Minutes of previous meeting

The minutes of the previous meeting were checked for accuracy. The Chairman signed the minutes as a true record of the previous meeting. There were no matters arising.

6. Appraisal 1 – olanzapine depot (ZypAdhera®)
Maintenance treatment of adult patients with schizophrenia, stabilised on oral olanzapine

The Chairman invited members to declare interests in either the applicant company or the medicine. There were none.

The Chairman welcomed delegates representing the applicant company, Eli Lilly.

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. The Chairman confirmed that the applicant company delegates would be invited to respond to and provide clarification of any issues raised. 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 and explained the reasons why members of the New Medicines Group had concluded that Olanzapine depot (ZypAdhera®) should not be recommended for use within NHS Wales for maintenance treatment of adult patients with schizophrenia sufficiently stabilised during acute treatment with oral olanzapine.

The Chairman opened the discussion and invited members to raise issues in relation to the clinical effectiveness. Members sought clarification in relation to compliance and patient sub-populations. The Chairman drew members attention to the medical expert opinion received. It was noted that NICE guidelines for schizophrenia had been highlighted; although not specified. One expert had commented on the disease prevalence and highlighted the potential for increased patient numbers. The medical expert view was that use of this medicine was considered limited due to the observations required after the injection had been administered. It was suggested that ZypAdhera® could be considered useful for patients who were non-compliant with medication; if it could be administered in an environment where the patient could be monitored for three hours post injection.

The Chairman invited comment on the case for cost effectiveness. Professor Phillips highlighted the levels of uncertainly in the economic model and questioned the rates of relapse

and discontinuation. The broader societal and budget impact issues were considered by members. The significant potential increase in patient numbers in 2011 compared to 2010 was noted. Councillor Meurig Hughes referred members to the submission from the patient organisation, Hafal and confirmed he had no issues of note.

The Chairman invited the applicant company delegates to respond to the issues raised and highlight any salient issues. It was suggested that ZypAdhera® represents a valuable treatment option for patients with moderate to severe schizophrenia when restricted to those receiving oral olanzapine who have problems with adherence and/or who express a choice for an olanzapine depot medication. It was acknowledged that the licence was not reflective of the trial undertaken and provided in the submission; however, the delegates considered the model was driven by anticipated clinical practice. The delegates responded to the issue of budget impact and clarified that a conservative approach had been adopted. It was confirmed that the company had restricted the submission to patients who are stabilised on oral olanzapine and who have been identified as high risk patients, those who have difficulty with adherence and/or are prone to recurrent relapse and exacerbation of symptoms.

Mr John Watkins joined the meeting and the Chairman confirmed that Mr Watkins would be unable to participate in the vote as he had not been present for the discussion in its entirety.

Prior to concluding the appraisal, the Chairman asked the company delegates to confirm 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 asked members to make a note of their comments on the aide-memoire and closed the appraisal.

Appraisal decision

The recommendation of AWMSG was announced:

Olanzapine depot (ZypAdhera®) is not recommended for use within NHS Wales for maintenance treatment of adult patients with schizophrenia sufficiently stabilised during acute treatment with oral olanzapine. The case for cost effectiveness has not been proven.

7. Appraisal 2 - epoetin theta (Eporatio®▼)

For the treatment of adult patients with symptomatic anaemia associated with chronic renal failure or those with non-myeloid malignancies receiving chemotherapy

The Chairman welcomed the delegates representing the applicant company. It was noted that Teva UK Limited had recently acquired Ratiopharm UK.

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

The Chairman alluded to his previous statement and confirmed it was pertinent to all appraisals.

The Chairman invited Dr Robert Bracchi, Chairman of the New Medicines Group, to set the context, summarise discussions at NMG and provide the rationale behind the preliminary recommendation to AWMSG that use of epoetin theta (Eporatio®▼) should be supported with restrictions as a treatment option.

The Chairman opened discussions and invited comments in relation to clinical effectiveness. The issue of bioequivalence was clarified. The Chairman drew members' attention to the views of the clinical experts. Darbepoetin was suggested as having an advantage in widespread rural areas and with the elderly patients, due to the fact it is longer-acting. One expert commented

that he would use the product if sizeable cost-savings could be shown provided efficacy and dosing frequency were maintained. It was also suggested there may be more pressure to consider it as a treatment option as blood supplies become tighter and the cost of blood and day-care increases. Another expert suggested such products would alleviate day-case unit capacity. Others suggested there would not be a large clinical demand for the product. One such expert suggested that the current practice of giving blood transfusions when clinically indicated was likely to remain the most cost effective approach.

The Chairman invited comments in relation to cost effectiveness. There was some concern expressed that tables 2 and 3 night be contradictory. Societal and budget impact issues were considered by the members. It was noted that two patient organisation submissions had been received (Myeloma UK and Leukaemia CARE) in relation to the treatment of symptomatic anaemia in adult cancer patients with non-myeloid malignancies receiving chemotherapy. Councillor Hughes acknowledged the comprehensive submissions and confirmed he had no further issues of note.

Prior to concluding the appraisal, the Chairman asked the company delegates to confirm that all issues had been adequately discussed and taken into account, and that the process had been fair and transparent. Confirmation was received.

The recommendation of AWMSG was announced:

Epoetin theta (Eporatio®▼) is recommended as an option for restricted use within NHS Wales for the treatment of adult patients with symptomatic anaemia associated with chronic renal failure only.

AWMSG is of the opinion that epoetin theta (Eporatio®▼) is not suitable for shared care within NHS Wales for the above indication.

Epoetin theta (Eporatio®▼) should be prescribed by brand name to avoid automatic substitution and therefore help with pharmacovigilance.

Epoetin theta (Eporatio®▼) is not recommended for use within NHS Wales for the treatment of symptomatic anaemia in adult cancer patients with non-myeloid malignancies receiving chemotherapy. The case for clinical effectiveness of epoetin theta (Eporatio®▼) has not been proven in this indication.

8 AWPAG update paper - Low Molecular Weight Heparin (LMWH)

The Chairman invited Dr Tessa Lewis, Chair of the All Wales Prescribing Advisory Group (AWPAG) to highlight to salient issues of Enc **4**/AWMSG/1010. Dr Lewis asked members to consider and support the interventions relating to LMWH to promote uptake of best practice and to reduce avoidable harm, waste and variation in NHS Wales.

Dr Lewis provided the background and confirmed that in March 2010 AWMSG had endorsed five recommendations addressing the prescribing of LMWH in NHS Wales. These covered the most common scenarios of LMWH prescribing. Dr Lewis informed members that AWPAG had worked with colleagues to address outstanding issues where professionals sought prescribing guidance.

It was noted that the paper is pertinent to Recommendation 19 of the AWMSG Medicines Strategy for Wales - *'AWMSG will work with clinical networks and Specialist groups to ensure that national clinical pathways and guidance include consistent advice on cost effective and evidence-based prescribing'.* Dr Lewis informed members that use of LMWH involves a diverse group of health professionals and patients and there is an education requirement to support the safe use of LMWH and to promote best practice.

Dr Lewis highlighted the aims of the document:

- To ensure that all patients receive appropriate anticoagulation in a timely manner
- To address prescribers' concerns relating to the safe prescribing of LMWH
- To promote consistent advice to patients via efficient and consistent clinical pathways for the prescribing and supply of LMWH
- To provide interim guidance to prescribers regarding the use of LMWH where the evidence base has yet to be established nationally

The Chairman opened the discussion and Dr Lewis responded to the issues raised. The Chairman concluded by confirming the support of AWMSG by endorsing the good prescribing practice. It was confirmed that the document would be made available on the AWMSG website and disseminated electronically to NHS Wales.

9 AWMSG sub-group constitution updates

The Chairman invited Mrs Kath Haines to highlight the updates to the constitutions of the New Medicines Group (NMG) and the All Wales Prescribing Advisory Group (AWPAG). Mrs Haines confirmed that the documents had been updated to reflect the organisational changes within NHS Wales and reflected the broadening of AWMSG's appraisal remit. The differences in the terms of office of the groups were noted. An amendment was noted in relation to the AWPAG constitution that membership should reflect local health boards and trusts and that the non-ABPI Wales non-voting member should read 'British Generics Manufacturing Association'. The Chairman closed the discussion by confirming that with these changes the constitutions of the AWMSG sub-groups (NMG and AWPAG) were endorsed by AWMSG.

10 Update on the ITS project – monitoring AWMSG recommendations

The Chairman invited Mrs Haines to provide an overview of Enc **6**/AWMSG/2010, the first of two papers currently in development that look at the usage of medicines appraised by AWMSG from date of licensing until 31st March 2010. Mr Haines clarified that the paper only included monitoring of medicines 'not recommended' by AWMSG for use in NHS Wales. The second paper would look at medicines 'recommended' for use in NHS Wales. Mrs Haines clarified the aim of the paper - to keep AWMSG informed of progress in relation to monitoring AWMSG recommendations, and to advise on actions that should be taken to reduce variance from AWMSG recommendations.

Mrs Haines reported that in September 2009 the Welsh Medicines Partnership had bid for additional funding from The Welsh Assembly Government's "Invest to Save" Fund to analyse prescribing data, promote effective prescribing across Wales and initiate a system to monitor the managed introduction of appraised medicines within NHS Wales. Members were informed that from 2003 to April 2010 AWMSG made 81 recommendations in relation to the use of new medicines in Wales. Of these recommendations:

37 had been supported for use within NHS Wales
19 had been supported with restrictions
25 had not been supported

Monitoring the usage of medicines not recommended by AWMSG, from date of licensing until 31st March 2010, had revealed a number of issues:

- It is not possible to monitor the usage of medicines for a particular indication because the data available currently does not link medicines usage to an indication.
- Medicines are being prescribed prior to consideration by AWMSG.
- Medicines that are not recommended by AWMSG are, in some cases, being prescribed after the negative recommendation has been issued to NHS Wales.

WMP concluded that in order to address the above issues the following actions should be recommended:

- Monitoring of AWMSG recommendations continues and information is fed back to NHS Wales.
- The status of AWMSG recommendations is made clear to NHS Wales.
- Consideration is given to the further development of Medusa to include information on indications for high cost medicines.
- Advice is provided on prescribing of medicines prior to appraisal by AWMSG.

Mrs Haines reported a detailed study had been undertaken in relation to the uptake of aliskiren (Rasilez®), an oral medication licensed in August 2007 for essential hypertension and not recommended by AWMSG for use in NHS Wales (AWMSG appraisal undertaken September 2009). Use of aliskiren had been identified during the two years prior to the AWMSG recommendation not to support its use. Further growth had continued following the AWMSG's recommendation and the cost for the two financial years 2008-9 and 2009-10 totalled £183,000. Mrs Haines ended her presentation by concluding that the results indicated that NHS Wales prescribing did not necessarily follow the advice issued by AWMSG and ratified by the Minister for Health and Social Services in all parts of Wales. The Chairman opened the discussion.

Members welcomed the information and considered it a useful tool for use at a local level to monitor compliance to national prescribing advice. Members supported the recommendations set out in the documentation, particularly with regard to continued monitoring and feedback. The Chairman acknowledged the input of the project lead, Mrs Cheryl Way, and concluded the discussions.

11 Update on the broadening of AWMSG appraisal process

An update of the appraisal documentation and process flow diagrams was provided to members for information. It was confirmed that the documentation had been posted on the AWMSG website to coincide with the implementation of AWMSG's broadened appraisal remit from 1st October 2010.

The Chairman confirmed the date of next AWMSG meeting:
Wednesday, 15th December 2010 at 10.30am in The Angel Hotel, Abergavenny

Subsequent meeting date:
Thursday, 17th February 2011 at 10.30am in The Angel Hotel, Abergavenny