

<b>Enclosure No:</b>	<b>1/AWMSG/0612</b>
<b>Agenda Item No:</b>	<b>5 – Minutes of previous meeting</b>
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## ALL WALES MEDICINES STRATEGY GROUP

### MINUTES OF THE AWMSG MEETING HELD ON WEDNESDAY 9<sup>th</sup> MAY 2012 COMMENCING 10.30 AM AT [THE ANGEL HOTEL](#), ABERGAVENNY, NP7 5EN

#### VOTING MEMBERS PRESENT:

Did not  
participate in

- |                           |  |   |
|---------------------------|--|---|
| 1. Prof Philip Routledge  | Chairman   |   |
| 2. Dr Fraser Campbell     | GP with prescribing lead role                        |   |
| 3. Dr Geoffrey Carroll    | Welsh Health Specialised Services Committee          |   |
| 4. Prof David Cohen       | Health Economist                                     |   |
| 5. Mrs Debbie Davies      | Representing other professions eligible to prescribe |   |
| 6. Mr Stefan Fec          | Community Pharmacist                                 |   |
| 7. Dr Bruce Ferguson      | Medical Director                                     |   |
| 8. Dr Karen Fitzgerald    | Consultant in Pharmaceutical Public Health           |   |
| 8. Mr Robert Holcombe     | Director of Finance                                  |   |
| 10. Dr Stuart Linton      | Hospital Consultant                                  |   |
| 11. Mrs Susan Murphy      | Senior Primary Care Pharmacist                       |   |
| 12. Mr Christopher Palmer | Lay member   |   |
| 13. Mr Paul Robinson      | ABPI Wales   |   |
| 14. Mr Christian Smith    | Senior Nurse   | 8 |
| 15. Dr John Watkins       | Consultant in Public Health Medicine                 |   |
| 16. Mr Roger Williams     | Senior Hospital Pharmacist                           |   |

#### IN ATTENDANCE:

17. Professor Roger Walker, Welsh Government
18. Mrs Karen Samuels, All Wales Therapeutics & Toxicology Centre
19. Mrs Ruth Lang, All Wales Therapeutics & Toxicology Centre
20. Dr Robert Bracchi, NMG Chairman

#### AWTTC APPRAISAL LEADS:

21. Mrs Sabrina Rind, Senior Appraisal Pharmacist
22. Dr David Jarrom, Senior Appraisal Scientist

## 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
AWTTC	All Wales Therapeutics & Toxicology Centre
CHMP	Committee for Medicinal Products for Human Use
DH	Department of Health
EMA	European Medicines Agency
FAR	Final Appraisal Recommendation
GP	General Practitioner
HAC	High Acquisition Cost
HB	Health Boards
MMPB	Medicines Management Programme Board
M&TCs	Medicines & Therapeutics Committees
NICE	National Institute for Health and Clinical Excellence
NMG	New Medicines Group
PAR	Preliminary Appraisal Recommendation
SMC	Scottish Medicines Consortium
TDAPG	Therapeutic Development Appraisal Partnership Group
T&FG	Task and Finish Group
WG	Welsh Government
WAPSU	Welsh Analytical Prescribing Support Unit
WMP	Welsh Medicines Partnership

### 1. Welcome and introduction

The Chairman welcomed members and confirmed that Mr Paul Robinson had been appointed ABPI Wales representative and was attending his first AWMSG meeting.

### 2. Apologies

Dr Philip Banfield, Hospital Consultant  
Mrs Ellen Lanham, Community Pharmacist  
Dr Emma Mason, Clinical Pharmacologist  
Dr Balwinder Bajal, Clinical Pharmacologist (deputy)

### 3. Declarations of interest

Mr Christian Smith declared a personal specific interest in Pfizer. The Chairman confirmed that Mr Smith would be excluded from participating in appraisal 3.

### 4. Chairman's report

It was reported, since the previous meeting, members had received an invitation to attend AWMSG's 10 Year Conference to be held on Thursday, 24<sup>th</sup> May at the Wales Millennium Stadium. It was announced, prior to the start of the Conference, the Minister for Health and Social Services would launch the All Wales Therapeutics & Toxicology Centre, which included the Welsh Medicines Partnership, the Welsh Medicines Resource Centre and Toxicology services provided by the National Poisons Information Centre. It was confirmed a copy of the conference programme had been circulated.

The Chairman confirmed that following discussions at the previous AWMSG meeting, the national audit – Towards more appropriate management of depression in a primary care setting – had been updated to reflect discussions at AWMSG and had been endorsed outside of the meeting by Chairman's action. Members were informed that the guidance on erectile dysfunction had been referred back to the All Wales Prescribing Advisory Group for clarification of wording in relation to the one outstanding recommendation. It was confirmed that AWPAG

had met on 26<sup>th</sup> April; the minutes were in the process of being finalised and an update report would be presented to AWMSG in June.

The Chairman reported at the February meeting that a proposal had been put to the Chairman of the National Medicines Management Programme Board (NMMPB) to establish an implementation group reporting to AWMSG which could encompass the role of the NMMPB. There were no further developments of note.

The Chairman reported that on 3<sup>rd</sup> May 2012 the service had been informed of ratification in relation to the following AWMSG recommendations:

**Linagliptin (Trajenta<sup>®</sup>▼)** is not recommended for use within NHS Wales for the treatment of type 2 diabetes mellitus to improve glycaemic control in adults as:

Monotherapy:

- in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to intolerance, or contraindicated due to renal impairment.

Combination therapy:

- in combination with metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control.

- in combination with a sulphonylurea and metformin when diet and exercise plus dual therapy with these medicinal products do not provide adequate glycaemic control

**Adalimumab (Humira<sup>®</sup>▼)** in combination with methotrexate is recommended as an option for use within NHS Wales for the treatment of active polyarticular juvenile idiopathic arthritis, in children and adolescents aged 4 to 17 years who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs. Adalimumab (Humira<sup>®</sup>▼) can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate.

AWMSG was of the opinion that adalimumab (Humira<sup>®</sup>▼) is suitable for specialist only prescribing within NHS Wales for the above indication.

**Esomeprazole (Nexium<sup>®</sup> IV)** is recommended as an option for use within NHS Wales for gastric antisecretory treatment when the oral route is not possible, such as gastro-oesophageal reflux disease (GORD) in patients with erosive reflux oesophagitis and/or severe symptoms of reflux for children and adolescents aged 1–18 years of age.

AWMSG was of the opinion that esomeprazole (Nexium<sup>®</sup> IV) is suitable for specialist only prescribing within NHS Wales for the above indication.

The Chairman confirmed, in the absence of a submission from the holder of the marketing authorisation, the following Statements of Advice had been ratified by Welsh Government and were therefore not available within NHS Wales:

**Fampridine (Fampyra<sup>®</sup>)** for improvement of walking in adult patients with multiple sclerosis with walking disability (EDSS 4-7).

**Etanercept (Enbrel<sup>®</sup>)** for the treatment of chronic severe plaque psoriasis in children and adolescents from the age of 6 years who are inadequately controlled by, or are intolerant to, other systemic therapies or phototherapies.

**Racecadotril (Hidrasec<sup>®</sup>)** granules for oral suspension for the complementary symptomatic treatment of acute diarrhoea in infants (older than 3 months), and in children, together with oral rehydration, and the usual support measures, when these measures alone are insufficient to control the clinical condition.

**Racecadotril (Hidrasec<sup>®</sup>)** capsules for the symptomatic treatment of acute diarrhoea in adults.

**Bismuth/metronidazole/tetracycline (Pylera<sup>®</sup>)** in combination with omeprazole for the eradication of *Helicobacter pylori* and prevention of relapse of peptic ulcers in patients with active, or a history of, *H. pylori* associated ulcers.

**Clevidipine (Cleviprex<sup>®</sup>)** for rapid reduction of blood pressure in the perioperative setting.

**Eculizumab (Soliris<sup>®</sup>)** for the treatment of patients with atypical haemolytic uraemic syndrome (aHUS).

**Triptorelin pamoate (Decapeptyl<sup>®</sup> SR)** 22.5 mg as an adjuvant treatment to radiotherapy in patients with high-risk localised or locally advanced prostate cancer.

**Fidaxomicin (Dificlr<sup>®</sup>)** for the treatment of adults with *Clostridium difficile* infections, also known as *C. difficile*-associated diarrhoea.

**Azilsartan medoxomil (Edarbi<sup>®</sup>)** for the treatment of essential hypertension in adults.

**Phentolamine mesylate (OraVerse<sup>®</sup>)** for reversal of soft tissue anaesthesia, and the associated functional deficits, resulting from an intraoral submucosal injection of a local anaesthetic containing a catecholamine vasoconstrictor following a routine dental procedure.

**Nepafenac (Nevanac<sup>®</sup>)** for reduction in the risk of postoperative macular oedema associated with cataract surgery in diabetic patients.

The Chairman confirmed a number of statements of advice were in preparation and statements relating to the following medicines would be forwarded to Welsh Government should a Form B or Form C submission not be received by WMP within the next fourteen days.

Mitotane (Lysodren<sup>®</sup>) for the symptomatic treatment of advanced (unresectable, metastatic or relapsed) adrenal cortical carcinoma. The effect of Lysodren on non-functional adrenal cortical carcinoma is not established.

Aminolevulinic acid) (Ameluz<sup>®</sup>) for the treatment of actinic keratosis of mild to moderate intensity on the face and scalp (Olsen grade 1 to 2).

Interferon beta-1a (Rebif<sup>®</sup>) for the treatment of patients with a single demyelinating event with an active inflammatory process, if alternative diagnoses have been excluded, and if they are determined to be at high risk of developing clinically definite multiple sclerosis.

Vandetanib (Caprelsa<sup>®</sup>) for the treatment of aggressive and symptomatic medullary thyroid cancer (MTC) in patients with unresectable locally advanced or metastatic disease. For patients in whom rearranged during transfection (RET) mutation is not known or is negative, a possible lower benefit should be taken into account before individual treatment decision.

The appraisals scheduled for the next meeting to be held in Cardiff on Wednesday, 20<sup>th</sup> June 2012 were announced:

**Appraisal 1: Full Submission**

**Belatacept (Nulojix<sup>®</sup>)** for prophylaxis of graft rejection in adults receiving a renal transplant, in combination with corticosteroids and a mycophenolic acid  
Applicant Company: Bristol-Myers Squibb Pharmaceuticals

**Appraisal 2: Full Submission**

**Rilpivirine (Edurant<sup>®</sup>)** in combination with other antiretroviral medicinal products for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in antiretroviral treatment naive adult patients with a viral load  $\leq 100,000$  HIV-1 RNA copies/ml

Applicant Company: Janssen-Cilag Ltd

**Appraisal 3: Limited submission**

**Nevirapine (Viramune<sup>®</sup>) 400 mg prolonged release tablets** in combination with other anti-retroviral medicinal products for the treatment of HIV-1 infected adults

Applicant Company: Boehringer Ingelheim Ltd

**Appraisal 4: Limited submission**

**Nevirapine (Viramune<sup>®</sup>) 50 mg, 100 mg, 400 mg prolonged release tablets** in combination with other anti-retroviral medicinal products for the treatment of HIV-1 infected adolescents and children three years and above and able to swallow tablets

Applicant Company: Boehringer Ingelheim Ltd

**Appraisal 5: Limited Submission**

**Rifaximin (Xifaxanta<sup>®</sup>▼)** for the treatment of travellers diarrhoea that is not associated with any of: fever, bloody diarrhoea, eight or more unformed stools in the previous 24 hours, occult blood or leucocytes in the stool. Rifaximin (Xifaxanta<sup>®</sup>) may shorten the duration of diarrhoea when this is associated with non-invasive strains of E.coli

Applicant Company: Norgine Pharmaceuticals Ltd

The Chairman reminded members to declare to AWTTTC any interests in relation to the appraisals scheduled. The Chairman invited patients, patient organisations and patient carers to submit their views and contact AWTTTC for further information in relation to the future work programme.

**5. Minutes of previous meeting**

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

**6. Appraisal 1: Full submission**

**Midazolam (Buccolam<sup>®</sup>▼)** for the treatment of prolonged, acute, convulsive seizures in infants, toddlers, children and adolescents (from 3 months to < 18 years). Buccolam must only be used by parents/carers where the patient has been diagnosed to have epilepsy. For infants between 3-6 months of age treatment should be in a hospital setting where monitoring is possible and resuscitation equipment is available.

Dr David Jarrom, AWTTTC assessment lead, joined members.

The Chairman welcomed delegates from the applicant company, ViroPharma Limited.

The Chairman invited members to declare any interests in either the applicant company or the medicine if they had not already done so. There were none.

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 Welsh Government officials, 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 invited Dr Jarrom to set the context of the appraisal. Dr Jarrom provided an overview of the submission as detailed in the [ASAR](#) and relayed the views of the [clinical experts](#).

Dr Bracchi reported that NMG acknowledged there were some methodological flaws in the submission, but held the view that a licensed product was welcomed. Dr Bracchi confirmed NMG had recommended that Midazolam (Buccolam<sup>®▼</sup>) should be available as an option for the indication being considered, and suggested that use should be monitored. It was confirmed that in forming their recommendation NMG had considered the safety issues relating to the unlicensed preparation.

The Chairman opened the discussion and members sought clarification in relation to the strength and concentration of the product, disposal requirements and associated costs relating to the pre-filled syringes, and the availability of training offered by the applicant company. Professor Cohen highlighted the limitations of the case for cost effectiveness, and informed members that the health economic model provided by the company had not included information relating to the whole of the licensed indication. There were no outstanding budget impact or societal issues of note. The patient representative drew member's attention to the salient issues within the patient organisation submission provided by Epilepsy Action Cymru.

The applicant company delegates responded to the issues highlighted by AWMSG in their discussion and highlighted that ViroPharma Limited had embarked on a large bespoke training programme. They confirmed there were no anticipated additional cost or issues relating to the disposal of the pre-filled syringes.

Prior to concluding the appraisal, the Chairman sought confirmation from the company delegates that the process had been fair and transparent. He thanked ViroPharma for engaging in the appraisal process.

#### **Appraisal decision subsequently announced**

The Chairman confirmed that having read the evidence and considered the various issues that arose during the discussion, AWMSG had agreed the following recommendation would be forwarded to Welsh Government:

**Midazolam (BUCCOLAM<sup>®▼</sup>) is recommended as an option for use within NHS Wales for the treatment of prolonged, acute, convulsive seizures in infants, toddlers, children and adolescents (from 3 months to < 18 years). For infants between 3-6 months of age treatment should be in a hospital setting where monitoring is possible and resuscitation equipment is available.**

**Midazolam (BUCCOLAM<sup>®▼</sup>) should be prescribed by brand name to reduce the risk of medication errors.**

#### **7. Appraisal 2: Limited submission**

**Fluorouracil/salicylic acid (Actikerall<sup>®</sup>)** for the topical treatment of slightly palpable and/or moderately thick hyperkeratotic actinic keratosis (grade I/II) in immunocompetent adult patients

The Chairman welcomed delegates from the applicant company, Almirall Limited.

The Chairman reminded members to declare any interests. There were none.

He referred to his previous statement 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 Welsh Government officials, 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 set the context of the appraisal and outlined the sequence of events. He confirmed that the application had been considered eligible for a limited submission. In line with

this process, evidence of budgetary impact in comparison to the existing comparator product(s) should be demonstrated. He directed members to consider the evidence and highlight any societal issues, take account of NMG's preliminary recommendation and the company response. He confirmed that clinical expert and patient views would be included, where available. He explained, in the event that AWMSG wished to explore any issues within the submission, then the applicant company delegates would be invited to provide clarification. However, if AWMSG considered there were no outstanding issues, they would retire to vote in private and agree the final recommendation, which would be subsequently announced and forwarded to Welsh Government for ratification. The Chairman reiterated that monitoring of budget impact would be essential and AWMSG reserved the right to request a full submission should the budget impact exceed that estimated in the limited submission.

Dr Jarrom set the context of the appraisal and highlighted relevant issues within the [ASAR](#). He confirmed that the submission had met the criteria for a limited submission in that the anticipated usage in NHS Wales was considered to be of minimal budgetary impact and the estimated difference in cost compared to the comparator/s was considered small. Dr Jarrom relayed the views of the [clinical experts](#) and confirmed that no patient submission had been received.

Dr Bracchi confirmed the view of NMG that fluorouracil/salicylic acid (Actikerall<sup>®</sup>) should be available as an option for the topical treatment of slightly palpable and/or moderately thick hyperkeratotic actinic keratosis (grade I/II) in immunocompetent adult patients

The Chairman invited members to raise any outstanding issues in relation to the limited submission. There was brief discussion which included duration of therapy, spontaneous regression rates and the terminology immunocompetence. The applicant company delegates responded to issues identified by AWMSG and were invited to highlight relevant aspects of their submission. There were no societal or budget impact issues of note.

Prior to concluding the appraisal, the Chairman asked the company delegates to confirm that all the outstanding issues had been addressed and they agreed that the process had been fair and transparent. The Chairman thanked Almirall Limited for engaging in the appraisal process and closed the appraisal.

### **Appraisal decision subsequently announced**

The Chairman confirmed that having read the evidence and considered the various issues that arose during the discussion, AWMSG had agreed the following recommendation would be forwarded to Welsh Government:

**Fluorouracil/salicylic acid (Actikerall<sup>®</sup>) is recommended as an option for use within NHS Wales for the topical treatment of slightly palpable and/or moderately thick hyperkeratotic actinic keratosis (grade I/II) in immunocompetent adult patients.**

### **8. Appraisal 3: Limited submission**

**Atorvastatin (Lipitor<sup>®</sup>▼)** chewable tablets as an adjunct to diet for reduction of elevated total cholesterol (total-C), LDL-cholesterol (LDL-C), apolipoprotein B, and triglycerides in adults, adolescents and children aged 10 years or older with primary hypercholesterolaemia including familial hypercholesterolaemia (heterozygous variant) or combined (mixed) hyperlipidaemia (corresponding to Types IIa and IIb of the Fredrickson classification) when response to diet and other non pharmacological measures is inadequate.

- To reduce total-C and LDL-C in adults with homozygous familial hypercholesterolaemia as an adjunct to other lipid-lowering treatments (e.g. LDL apheresis) or if such treatments are unavailable.

- Prevention of cardiovascular events in adult patients estimated to have a high risk for a first cardiovascular event, as an adjunct to correction of other risk factors.

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The Chairman reminded members to declare any interests. Mr Christian Smith had declared a personal specific interest in Pfizer earlier in the meeting and left the room.

The Chairman referred to his previous statement, 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 Welsh Government officials, 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 set the context of the appraisal and outlined the sequence of events. He confirmed that the application had been considered eligible for a limited submission. In line with this process, evidence of budgetary impact in comparison to the existing comparator product(s) should be demonstrated. He directed members to consider the evidence and highlight any societal issues, take account of NMG's preliminary recommendation and the company response. He confirmed that clinical expert and patient views would be included, where available. He explained, in the event that AWMSG wished to explore any issues within the submission, then the applicant company delegates would be invited to provide clarification. However, if AWMSG considered there were no outstanding issues, they would retire to vote in private and agree the final recommendation, which would be subsequently announced and forwarded to Welsh Government for ratification. The Chairman reiterated that monitoring of budget impact would be essential and AWMSG reserved the right to request a full submission should the budget impact exceed that estimated in the limited submission.

The Chairman introduced Mrs Sabrina Rind, AWTTTC Senior Appraisal Pharmacist and lead for this appraisal. Mrs Rind provided an overview of the [ASAR](#) highlighted the salient issues. She explained that atorvastatin chewable tablets (Lipitor<sup>®</sup>▼) for the above indication had met the following criteria for eligibility for a limited submission in that it was a new formulation with a pro-rata or lower cost per treatment, the anticipated usage in NHS Wales was considered to be of minimal budgetary impact and the estimated difference in cost compared to atorvastatin (Lipitor<sup>®</sup>▼) film coated tablets was considered small. The views of the [clinical experts](#) relayed and it was noted that no patient submission had been received.

Dr Bracchi confirmed that NMG considered that atorvastatin (Lipitor<sup>®</sup>▼) chewable tablets for the indication being considered should be available within NHS Wales as an option, and their preliminary recommendation was to support the use of the medicine for the stated indication.

There were no outstanding clinical effectiveness issues of note. The Chairman reiterated that cost effectiveness was not considered as part of a limited submission, and asked members to raise any issues relating to budget impact. There were no social or budget issues raised by members. The lack of safety data relating to use in children was noted and the company delegates were asked to justify the lack of evidence to support the use of the medicine in this patient population. The company delegates responded to the issues raised and, prior to the conclusion of the appraisal, confirmed that the process had been fair and transparent.

The Chairman thanked Pfizer for engaging in the appraisal process and members left the room to vote in camera.

### **Appraisal decision subsequently announced**

The Chairman confirmed that having read the evidence and considered the various issues that arose during the discussion, AWMSG had agreed the following recommendation would be forwarded to Welsh Government:



**Atorvastatin (Lipitor<sup>®</sup>▼) chewable tablets are recommended as an option for use within NHS Wales**

- **as an adjunct to diet for reduction of elevated total cholesterol (total-C), LDL-cholesterol (LDL-C), apolipoprotein B, and triglycerides in adults, adolescents and children aged 10 years or older with primary hypercholesterolaemia including familial hypercholesterolaemia (heterozygous variant) or combined (mixed) hyperlipidaemia (corresponding to types IIa and IIb of the Fredrickson classification) when response to diet and other non-pharmacological measures is inadequate.**
- **to reduce total-C and LDL-C in adults with homozygous familial hypercholesterolaemia as an adjunct to other lipid-lowering treatments (e.g. LDL apheresis) or if such treatments are unavailable.**
- **for the prevention of cardiovascular events in adult patients estimated to have a high risk for a first cardiovascular event, as an adjunct to correction of other risk factors.**

The Chairman confirmed that the final appraisal recommendations would be forwarded to the relevant companies on or before Wednesday, 16<sup>th</sup> May 2012. He confirmed that the applicant companies had until Wednesday, 23<sup>rd</sup> May to accept the recommendation or lodge a request for an independent review, the grounds for which should be submitted in writing to the Chairman via the All Wales Therapeutics & Toxicology Centre. He explained the process would not be delayed if the companies failed to respond by the deadline. Subject to receiving a request for an independent review within the appropriate timelines, the recommendation would be passed to Welsh Government. The Chairman informed the company delegates they would be informed when ratification of AWMSG's recommendation had been received.

The Chairman thanked the applicant companies for engaging with the AWMSG process and confirmed that the appraisal proceedings had been concluded.

**9. Date of next meeting**

The Chairman confirmed the date of the next meeting - Wednesday, 20<sup>th</sup> June 2012 in Cardiff and the meeting closed.