

| | |
|------------------------|---|
| Enclosure No: | 1/AWMSG/0713 |
| Agenda Item No: | 5 – Minutes of previous meeting |
| Author: | Chairman, AWMSG |
| Contact: | Tel: 029 20716900 E-Mail: awttc@wales.nhs.uk |

ALL WALES MEDICINES STRATEGY GROUP (AWMSG)

MINUTES OF THE AWMSG MEETING HELD ON WEDNESDAY 12th JUNE 2013 COMMENCING 10.30 AM AT [THE ANGEL HOTEL](#), ABERGAVENNY, NP7 5EN

VOTING MEMBERS PRESENT:

**Did not
participate in**

- | | | | |
|-----|----------------------------|---|---|
| 1. | Professor Philip Routledge | Chairman | |
| 2. | Professor David Cohen | Health Economist | |
| 3. | Mrs Debbie Davies | Healthcare Professional eligible to prescribe | 8 |
| 4. | Mr Stuart Davies | Finance Director | |
| 5. | Dr Karen Fitzgerald | Consultant in Pharmaceutical Public Health | |
| 6. | Ms Ellen Lanham | Community Pharmacist | |
| 7. | Dr Emma Mason | Clinical Pharmacologist | |
| 8. | Mrs Susan Murphy | Managed Sector Primary Care Pharmacist | |
| 9. | Mr Christopher Palmer | Lay Member | |
| 10. | Mr Christian Smith | Senior Nurse representative | |
| 11. | Mr Rob Thomas | ABPI Cymru Wales | |
| 12. | Professor John Watkins | Public Health Wales | |
| 13. | Dr William Whitehead | GP with Prescribing Lead role | |
| 14. | Mr Roger Williams | Managed Sector Hospital Pharmacist | |

IN ATTENDANCE:

16. Professor Roger Walker, Chief Pharmaceutical Officer, Welsh Government
17. Dr Robert Bracchi, NMG Chairman
18. Mr Jamie Hayes, Head of Communication & Implementation, AWTTTC
19. Mrs Ruth Lang, Head of Liaison & Administration, AWTTTC

ALL WALES THERAPEUTICS & TOXICOLOGY CENTRE (AWTTC) APPRAISAL LEADS:

- 20. Mr Anthony Williams, Senior Appraisal Pharmacist
- 21. 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 |
| BMA | British Medical Association |
| CHMP | Committee for Medicinal Products for Human Use |
| DH | Department of Health |
| EMA | European Medicines Agency |
| FAR | Final Appraisal Recommendation |
| FDA | US Food and Drug Administration |
| GP | General Practitioner |
| HAC | High Acquisition Cost |
| HB | Health Boards |
| HTA | Health Technology Appraisal |
| IR | Independent Review |
| MHRA | Medicines and Healthcare products Regulatory Agency |
| 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 |
| WPAS | Welsh Patient Access Scheme |

1. Welcome and introduction

The Chairman welcomed AWMSG members and members of the public.

2. Apologies

Dr Geoffrey Carroll (Welsh Health Specialised Services Committee representative)
Dr Fraser Campbell (Dr Bill Whitehead deputising)
Dr Brendan Lloyd (Medical Director representative)
Dr Stuart Linton (Hospital Consultant representative)
Dr Richard Moore (Hospital Consultant deputy representative)

3. Declarations of interest

The Chairman reminded members to declare any interests pertinent to the agenda. The Chairman declared a non-specific, non-personal interest in AstraZeneca UK Ltd – a training post in Clinical Pharmacology had been part funded by AstraZeneca in 2012-2013. He informed members that he would chair the appraisal but would not participate in the vote. Mr Rob Thomas declared a personal non-specific interest in appraisal 2 and the Chairman confirmed that Mr Thomas would not participate in this appraisal.

4. Chairman's report

The Chairman confirmed that appraisal 3, C1-esterase inhibitor (Berinert) for the treatment of acute episodes of hereditary angioedema type I and II (HAE) would be conducted in private as the submission is associated with a Wales Patient Access Scheme containing commercially sensitive information. He confirmed that all three recommendations would be announced in public.

The Chairman informed members that at a recent meeting with Mark Drakeford, Minister for Health and Social Services, he had been asked to relay the Minister's thanks to members for their contribution to AWMSG in advising Welsh Government.

On 23rd May the Service was informed that three recommendations had been ratified by the Minister for Health and Social Services.

Linagliptin (Trajenta[®]▼) is recommended as an option 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;

as 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; and
- in combination with insulin with or without metformin, when this regimen alone, with diet and exercise, does not provide adequate glycaemic control.

Glycopyrronium bromide (Seebri[®] Breezhaler[®]▼) is recommended as an option for use within NHS Wales as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease.

Aztreonam lysine (Cayston[®]) is recommended as an option for restricted use within NHS Wales. This recommendation applies only in circumstances where the approved Wales Patient Access Scheme is utilised. **Aztreonam lysine (Cayston[®]) should be restricted** for third-line use in the following subpopulation within its licensed indication for suppressive therapy of chronic pulmonary infections due to *Pseudomonas aeruginosa* in patients with cystic fibrosis aged six years and older:

- Patients in whom nebulised colistimethate sodium and nebulised tobramycin are not tolerate or are not providing satisfactory therapeutic benefit.

Aztreonam lysine (Cayston[®]) is not recommended for use within NHS Wales outside of this subpopulation.

It was reported that subsequent to the appraisal of pazopanib (Votrient[®]▼), GlaxoSmithKline Limited had requested a review of AWMSG's recommendation. It was confirmed the appraisal process had been suspended and the grounds for review considered by the AWMSG Steering Committee on 29th May. The Chairman relayed the view of the AWMSG Steering Committee that a review should be undertaken, and confirmed that AWMSG would reconsider their recommendation in light of the review at a future meeting, yet to be scheduled.

The Chairman announced that the appraisal of nepafenac (Nevanac[®]) for reduction in the risk of postoperative macular oedema associated with cataract surgery in diabetic patients had been postponed to July.

Members were informed that ratification of the final appraisal recommendations announced in May had not been received. The Chairman reported that subsequent to the appraisal of

ivacaftor (Kalydeco) for the treatment of patients with cystic fibrosis and the G551D mutation in the CFTR gene, the Minister for Health and Social Services had issued a statement confirming that the thirteen eligible patients in Wales would have access to the medicine. Members were informed that the Chief Pharmaceutical Officer had been asked by the Minister to set up a review of AWMSG's policy for appraising orphan and ultra orphan medicines.

The Chairman announced the statements of advice recently ratified by Welsh Government and issued in the absence of a submission from the holder of the licence within the appropriate timescale. It was confirmed the following medicines are not endorsed for use within NHS Wales:

Hydromorphone hydrochloride (Palladone[®]) injection for the relief of severe pain in cancer. Hydromorphone hydrochloride is indicated in adults and adolescents aged > 12 years.

Everolimus (Votubia[®]) for the treatment of adult patients with renal angiomyolipoma associated with tuberous sclerosis complex who are at risk of complications (based on factors such as tumour size or presence of aneurysm, or presence of multiple or bilateral tumours) but who do not require immediate surgery.

Linacotide (Constella[®]) for the symptomatic treatment of moderate to severe irritable bowel syndrome with constipation in adults.

Tapentadol (Palexia[®]) oral solution for the relief of moderate to severe acute pain in adults, which can be adequately managed only with opioid analgesics.

Oxycodone (OxyNorm Dispersa[®]) orodispersible tablets for the treatment of moderate to severe pain in patients with cancer and postoperative pain and treatment of severe pain requiring the use of a strong opioid.

Ciprofloxacin/dexamethasone (Cilodex[®]) for the treatment of the following infections in adults and children: acute otitis media in patients with tympanostomy tubes (AOMT); acute otitis externa (AOE). Consideration should be given to official guidance on the appropriate use of antibacterial agents.

The Chairman announced seven submissions scheduled for appraisal at the next AWMSG meeting to be held in Cardiff on Wednesday, 17th July 2013:

1. Full Submission

Lapatinib (Tyverb[®]) for the treatment of adult patients with breast cancer, whose tumours overexpress HER2 (ErbB2), in combination with capecitabine for patients with advanced or metastatic disease with progression following prior therapy, which must have included anthracyclines and taxanes and therapy with trastuzumab in the metastatic setting
Applicant Company: GlaxoSmithKline

2: Full Submission

Nepafenac (Nevanac[®]) for reduction in the risk of postoperative macular oedema associated with cataract surgery in diabetic patients
Applicant Company: Alcon Laboratories (UK) Ltd

3: Full Submission

Ulipristal acetate (Esmya[®]) for the pre-operative treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age. The duration of treatment is limited to 3 months
Applicant Company: Gedeon Richter (UK) Ltd

4: Limited Submission

Adalimumab (Humira®) for the treatment of severe active Crohn's disease in paediatric patients (6 to 17 years of age) who have had an inadequate response to conventional therapy including primary nutrition therapy, a corticosteroid, and an immunomodulator, or who are intolerant to or have contraindications for such therapies

Applicant Company: AbbVie Ltd

5: Limited Submission

Adalimumab (Humira®) in combination with methotrexate for the treatment of active polyarticular juvenile idiopathic arthritis, in children aged 2-4 years who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs). Adalimumab can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate. Adalimumab has not been studied in children aged less than 2 years

Applicant Company: AbbVie Ltd

6: Limited Submission

Tenofovir disoproxil fumarate (Viread®) in combination with other antiretroviral medicinal products for the treatment of HIV-1-infected paediatric and adolescent patients aged 2 to < 18 years, with NRTI resistance or toxicities precluding the use of first line agents. The choice of tenofovir disoproxil fumarate to treat antiretroviral-experienced patients with HIV-1 infection should be based on individual viral resistance testing and/or treatment history of patients

Applicant Company: Gilead Sciences Ltd

7: Limited Submission

Tenofovir disoproxil fumarate (Viread®) for the treatment of chronic hepatitis B in adolescents 12 to < 18 years of age with compensated liver disease and evidence of immune active disease, i.e. active viral replication, persistently elevated serum ALT levels and histological evidence of active inflammation and/or fibrosis

Applicant Company: Gilead Sciences Ltd

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

Members were informed there would be no meeting in August and no public meeting in September. The Chairman informed members that the date of 4th September would be used for purposes such as training and further details would follow.

The Chairman concluded his report by expressing personal thanks to Dr Tessa Lewis who has served two terms of office on AWPAG and who has very successfully chaired the group over the last few years. The Chairman confirmed that Dr Lewis would continue to work as part of the team at the All Wales Therapeutics & Toxicology Centre and will be presenting the minutes of the AWPAG meeting held last week at the next AWMSG meeting. The Chairman announced that Mrs Louise Howard Baker from Betsi Cadwaladr UHB will be stepping up from Vice Chair and will take on the role as AWPAG Chair.

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 meeting.

**6. Appraisal 1 – Full submission
Ceftaroline fosamil (Zinforo®) for the treatment of the following infections: complicated skin and soft-tissue infections (cSSTI) and community-acquired pneumonia (CAP)**

The Chairman welcomed representatives from the applicant company, AstraZeneca UK Ltd.

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, 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 David Jarrom, AWTTTC assessment lead, to set the context of the appraisal. Dr Jarrom presented an overview of the submission as detailed in the ASAR and relayed the views of the clinical experts. Dr Jarrom highlighted that the applicant company had only submitted evidence for a sub-population and use outside of this group of patients could not be considered. Members were informed that a patient organisation submission had not been received.

The Chairman invited Dr Bracchi, NMG Chairman, to provide a brief overview of the relevant issues identified in the preliminary appraisal. Dr Bracchi briefly summarised the issues discussed at NMG and relayed the preliminary recommendation of NMG that ceftaroline fosamil (Zinforo®) should be supported as an option for restricted use within NHS Wales.

The Chairman invited comment in relation to the case for clinical effectiveness. There was discussion over resistance patterns and adverse events. It was noted that the company submission was restricted to a sub-set of the licensed indication.

The Chairman invited Professor Cohen to comment on the case for cost-effectiveness. Professor Cohen explained the reasons why cost minimisation analysis was not the preferred technique for health economic evaluation. He highlighted the limitations in the case submitted for cost effectiveness. The company representative acknowledged the limitations.

The Chairman referred members to the comprehensive clinical expert summary. There were no societal or budget impact issues of note.

The Chairman referred to the applicant company response to the preliminary recommendation and offered opportunity to the delegates to highlight salient issues. Prior to concluding the discussion, the Chairman sought confirmation from the company delegates that the process had been fair and transparent. He thanked AstraZeneca UK Ltd for engaging in the appraisal process and proceeded to the next appraisal.

Appraisal decision subsequently announced:

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

Ceftaroline fosamil (Zinforo®) is recommended as an option for restricted use within NHS Wales.

Ceftaroline fosamil (Zinforo^{®▼}) should be restricted to use for the treatment of complicated skin and soft tissue infections in patients where methicillin-resistant *S. aureus* (MRSA) is suspected, only in the following settings:

- For infections caused by Gram-positive pathogens, only if intravenous (IV) vancomycin or IV teicoplanin is inappropriate, has not been tolerated or treatment modification is required; and IV daptomycin or IV linezolid is normally used.
- For mixed infections caused by common Gram-positive and Gram-negative pathogens (excluding extended-spectrum beta-lactamase-producing organisms, AmpC-producing organisms and non-fermenter Gram-negative organisms, such as *Pseudomonas aeruginosa*), only if IV vancomycin in combination with IV co-amoxiclav or IV teicoplanin in combination with IV co-amoxiclav is inappropriate, has not been tolerated or treatment modification is required; and IV daptomycin in combination with IV co-amoxiclav or IV linezolid in combination with IV co-amoxiclav is normally used.

Ceftaroline fosamil (Zinforo^{®▼}) is not recommended for use within NHS Wales for the treatment of complicated skin and soft tissue infections outside of these settings.

Ceftaroline fosamil (Zinforo^{®▼}) is not recommended for use within NHS Wales for the treatment of community-acquired pneumonia.

7. Appraisal 2 – Full submission

Adalimumab (Humira[®]) for the treatment of adults with severe axial spondyloarthritis without radiographic evidence of ankylosing spondylitis but with objective signs of inflammation by elevated CRP and/or MRI, who have had an inadequate response to, or are intolerant to nonsteroidal anti-inflammatory drugs

The Chairman welcomed representatives from the applicant company, AbbVie Ltd

The Chairman invited members to declare any interests in either the applicant company or the medicine if they had not already done so. No further declarations were made and Mr Rob Thomas left the meeting.

The Chairman invited Mr Tony Williams, AWTTTC assessment lead, to set the context of the appraisal. Mr Williams presented an overview of the submission as detailed in the ASAR and relayed the views of the clinical experts. Members were informed a patient organisation submission had been received from the National Ankylosing Spondylitis Society.

The Chairman invited Dr Bracchi, NMG Chairman, to provide a brief overview of the relevant issues identified in the preliminary appraisal. Dr Bracchi briefly summarised the issues discussed at NMG and highlighted NMG's concerns in relation to treatment review. Dr Bracchi confirmed that NMG had considered the evidence provided in the submission supported use of the medicine in Wales.

Members discussed issues relating to the case for clinical effectiveness. Clarification was sought over the reporting of adverse events and the safety profile. There was discussion over response rates in the trial populations. The Chairman referred members to the clinical expert views. There was discussion in relation to prevalence and the uncertainties highlighted by the experts. Professor Cohen commented on the case for cost-effectiveness. There was discussion over the differences in treatment costs and clarification was sought in relation to how the estimates were derived. The projected budget impact was noted. Mr Palmer highlighted the salient issues within the patient organisation submission. Members of the patient organisation clearly supported adalimumab (Humira[®]) as an additional treatment option. Mr Palmer alluded to the societal issues within the patient organisation submission and these were noted.

The Chairman referred to the applicant company response to the preliminary recommendation and offered opportunity to the delegates to highlight any additional information. Prior to concluding the discussion, the Chairman sought confirmation from the company delegates that the process had been fair and transparent. He thanked AbbVie Ltd for engaging in the appraisal process and proceeded to the next appraisal.

Appraisal decision subsequently announced:

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

Adalimumab (Humira[®]) is recommended for use within NHS Wales for the treatment of adults with severe axial spondyloarthritis without radiographic evidence of ankylosing spondylitis but with objective signs of inflammation by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI), who have had an inadequate response to, or are intolerant to non steroidal anti-inflammatory drugs (NSAIDs).

Members of the public left the meeting.

**8. Appraisal 3 – Full submission – proceedings conducted in private
C1-esterase inhibitor (Berinert[®]) for the treatment of acute episodes of hereditary
angioedema type I and II (HAE)**

The Chairman welcomed representatives of the applicant company CSL Behring UK Ltd. 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 repeated the statement announced at the commencement of the appraisal session and confirmed it was pertinent to all appraisals. Mrs Debbie Davies left the meeting and did not take part in the subsequent vote on this appraisal.

The Chairman invited Mr Tony Williams, AWTTTC assessment lead, to set the context of the appraisal. Mr Williams presented an overview of the submission as detailed in the ASAR and relayed the views of the clinical experts. Members were informed that a patient organisation submission had been received from the Hereditary Angioedema Patient Association (HAE UK).

The Chairman invited Dr Bracchi, NMG Chairman, to provide a brief overview of the relevant issues identified in the preliminary appraisal. Dr Bracchi briefly summarised the issues discussed at NMG and relayed the view of NMG members that C1-esterase inhibitor (Berinert[®]) should be recommended as an option for use within NHS Wales for the indication under consideration.

The Chairman invited comment in relation to the case for clinical effectiveness. The Chairman referred members to the clinical expert summary and asked members to highlight any outstanding issues. There were none. Professor Cohen commented on the case for the cost-effectiveness of the medicine. Mr Chris Palmer highlighted the salient issues within the patient organisation submission. Individual patient stories had been submitted and noted by members. The patient submission supported the use of C1-esterase inhibitor (Berinert[®]) as an additional treatment option; no disadvantages were highlighted in their submission. Improvements to patients' quality of life were noted.

The Chairman referred to the applicant company response to the preliminary recommendation and offered opportunity to the delegates to highlight any additional information. Prior to concluding the discussion, the Chairman sought confirmation from the company delegates that the process had been fair and transparent. He thanked CSL Behring UK Ltd 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, the following recommendation would be forwarded to Welsh Government:

C1-esterase inhibitor (Berinert®) is recommended as an option for use within NHS Wales for the treatment of acute episodes of hereditary angioedema type I and II.

This recommendation applies only in circumstances where the approved Wales Patient Access Scheme is utilised.

9. Date of next meeting:

The Chairman confirmed the date of the next AWMSG meeting on **Wednesday, 17th July 2013 in Cardiff (commencing 9.30 am)** and closed the meeting.