

Enclosure No:	1/AWMSG/0719
Agenda Item No:	1 – Minutes of previous meeting
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ALL WALES MEDICINES STRATEGY GROUP (AWMSG)

Minutes of the AWMSG meeting held Wednesday, 19 June 2019 commencing 10.30 am at the Copthorne Hotel, Copthorne Way Culverhouse Cross, Cardiff, CF5 6DH

VOTING MEMBERS PRESENT:

**Did not
participate in**

- | | | |
|-----|-----------------------|--|
| 1. | Prof John Watkins | Chairman |
| 2. | Dr Cath Bale | Hospital Consultant |
| 3. | Dr Balwinder Bajaj | Clinical Pharmacologist |
| 4. | Dr Jeremy Black | General Practitioner |
| 5. | Mr Hywel Pullen | Director of Finance |
| 6. | Mrs Susan Murphy | Primary Care Pharmacist |
| 7. | Ms Cathy Wynne | Other professions eligible to prescribe |
| 8. | Mr Stefan Fec | Community Pharmacist |
| 9. | Prof Dyfrig Hughes | Health Economist |
| 10. | Mrs Louise Williams | Senior Nurse |
| 11. | Mr Cliff Jones | Lay Member |
| 12. | Mr John Terry | Managed Sector Secondary Care Pharmacist |
| 13. | Prof Stephen Monaghan | Consultant in Public Health Medicine |

In attendance:

Dr James Coulson, Chairman NMG
Mr Tony Williams, Senior Pharmacist Team Leader, AWTTTC
Mrs Ruth Lang, Senior Liaison Manager, AWTTTC
Dr Jessica Davis, Senior Scientist, AWTTTC

AWTTTC Leads:

Mrs Helen Adams, Senior Pharmacist
Miss Shaila Ahmed, Pharmacist
Ms Sabrina Rind, Senior Pharmacist

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
CAPIG	Clinical and Patient Involvement Group
CEPP	Clinical Effectiveness Prescribing Programme
CHMP	Committee for Medicinal Products for Human Use
DoH	Department of Health
EMA	European Medicines Agency
EMIG	Ethical Medicines Industry Group
EOL	End of life
FAR	Final Appraisal Recommendation
FDA	US Food and Drug Administration
GP	General Practitioner
HAC	High Acquisition Cost
HB	Health Board
HST	Highly Specialised Technology
HTA	Health Technology Appraisal
IR	Independent Review
MHRA	Medicines and Healthcare products Regulatory Agency
M&TCs	Medicines & Therapeutics Committees
NICE	National Institute for Health and Care Excellence
NMG	New Medicines Group
NPI	National Prescribing Indicator
PAMS	Patient Access to Medicines Service
PAR	Preliminary Appraisal Recommendation
PAS	Patient Access Scheme
PPRS	Prescription Price Regulation Scheme
SMC	Scottish Medicines Consortium
SPC	Summary of Product Characteristics
TDAPG	Therapeutic Development Appraisal Partnership Group
T&FG	Task and Finish Group
UHB	University Health Board
WAPSU	Welsh Analytical Prescribing Support Unit
WCPPE	Welsh Centre for Pharmacy Postgraduate Education
WeMeReC	Welsh Medicines Resource Centre
WG	Welsh Government
WHO	World Health Organization
WHSSC	Welsh Health Specialised Services Committee
WPAS	Wales Patient Access Scheme

1. Welcome and introduction

The Chair opened the meeting and welcomed members.

2. Apologies

Prof Iolo Doull, WHSSC
Mr Farhan Mughal, ABPI

3. Declarations of interest

Members were reminded to declare any interests. There were none.

4. Minutes of previous meeting

The draft minutes of the previous meeting were checked for accuracy and approved.

5. Chair's report (verbal update)

The Chair announced that AWMSG's Patient and Public Interest Group (PAPIG) had met on 20 May 2019 with presentations from Dr Philip Webb (Velindre) on RITA, a virtual assistant to support patients and respond to enquiries, and Ceri Philips (Aneurin Bevan) on antimicrobials. The Chair reminded members that there is an open invitation for patients and the public to attend this meeting.

The Chair informed members that in support of the medicines safety agenda, representatives from AWTTTC had demonstrated a medication safety dashboard at the Chief Pharmacist Symposium at Cardiff on 16 May 2019. The dashboard measures the connection/reports the relationship between medicine incidents and admissions in secondary care and gives a baseline for monitoring the safety strategy success over subsequent years.

It was reported that representatives from AWTTTC had attended the National Urdd Eisteddfod in Cardiff Bay on 30 May 2019 to engage with the general public, encourage their involvement and raise awareness of the work of AWTTTC and AWMSG. A news article has been published on the AWTTTC website.

The Chair confirmed the AWMSG Steering Committee had met on 4 June 2019. Members were informed that AWTTTC had been tasked by the Steering Committee to consider the feasibility of reviewing pre-2011 AWMSG recommendations. In consultation with WHSSC, AWTTTC proposed a process for reviewing medicines appraised pre-2011 which was approved by the Steering Committee. The Chair confirmed that all positive and negative appraisal recommendations would remain unchanged unless a reappraisal had been undertaken by AWMSG.

The Chair referred to the on-going review of the role and remit of AWMSG by Welsh Government and it was noted that the findings of the review had yet to be published.

The Chair announced that Welsh Government had ratified AWMSG's recommendations from the meeting held in May. It was confirmed that the applicant companies had been informed and the advice published on the AWMSG website:

Doxylamine succinate/pyridoxine hydrochloride (Xonvea®) is not recommended for use within NHS Wales for the treatment of nausea and vomiting of pregnancy (NVP) in women who do not respond to conservative management. The cost-effectiveness data presented in the submission were insufficient for AWMSG to recommend its use.

Fingolimod (Gilenya®) is recommended as an option for use within NHS Wales as a single disease modifying therapy in highly active relapsing remitting multiple sclerosis for the following groups of paediatric patients aged 10–17 years: patients with highly active disease despite a full and adequate course of treatment with at least one disease modifying therapy; or patients with rapidly evolving severe relapsing remitting multiple sclerosis defined by 2 or more disabling relapses in one year, and with 1 or more gadolinium enhancing lesions on brain MRI or a significant increase in T2 lesion load as compared to a previous recent MRI. This recommendation applies only in circumstances where the approved Patient Access Scheme (PAS) is utilised or where the list/contract price is equivalent or lower than the PAS price.

The Chair confirmed a number of statements of advice had been published since the previous meeting due to non-engagement by the marketing authorisation holder within the required timescale and these medicines cannot be endorsed for use within NHS Wales.

Brentuximab vedotin (Adcentris®) for adult patients with previously untreated CD30+ Stage IV Hodgkin lymphoma (HL) in combination with doxorubicin, vinblastine and dacarbazine (AVD)

Dasatinib (Sprycel®) for the treatment of paediatric patients with newly diagnosed Philadelphia chromosome-positive (Ph+) acute lymphoblastic leukaemia (ALL) in combination with chemotherapy

Golimumab (Simponi®) in combination with methotrexate is indicated for the treatment of polyarticular juvenile idiopathic arthritis in children 2 years of age and older, who have responded inadequately to previous therapy with methotrexate

The Chair announced the appraisal scheduled for the next AWMSG meeting on 17 July 2019 in the Copthorne Hotel, Cardiff:

A full submission for buprenorphine (Buvidal®) for the treatment of opioid dependence within a framework of medical, social and psychological treatment.

Applicant company: Camurus Ltd

Members were reminded to declare any personal or non-personal interests ahead of the next meeting. Patients, patient organisations and patient carers were invited to submit their views on these medicines or contact AWTTC for further information on the appraisal process and future work programme.

Appraisal 1: Limited Submission

6. **Rufinamide (Inovelon®)** for use as an adjunctive therapy in the treatment of seizures associated with Lennox-Gastaut syndrome in patients 1 year of age to less than 4 years of age.

The Chair welcomed delegates from Eisai Ltd.

The Chair invited members to declare any interests in either the applicant company or the medicine if they had not already done so. No interests were declared.

The Chair announced 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 Chair set the context of the limited submission and confirmed that evidence of clinical effectiveness and budgetary impact in comparison to any comparator product(s) should be demonstrated. It was confirmed that monitoring of budget impact would be essential and AWMSG reserved the right to request a full submission if the budget impact exceeded that estimated in the submission.

The appraisal lead set the context of the appraisal and relayed the key aspects of the submission as outlined in the ASAR. It was confirmed that a limited submission had been considered appropriate, as this was a minor licence extension with an anticipated minimal budgetary impact. The submission is restricted to where other adjunctive treatments have proved suboptimal or have not been tolerated, in line with AWMSG's recommendation for patients aged four years and older. The submission included extrapolation of efficacy data from patients aged four years and older, which was endorsed by the EMA. Rufinamide has a designated EMA orphan status and AWTTC considered that rufinamide meets the AWMSG criteria for an orphan medicine. Rufinamide for the indication under consideration is

recommended for restricted use in NHS Scotland.

The NMG Chair confirmed that NMG supported the restricted use of this medicine in NHS Wales for the indication stated. NMG restricted the recommendation for use where other adjunctive treatments have proved sub-optimal or have not been tolerated.

The Chair reiterated that rufinamide meets AWMSG's criteria for appraising orphan medicines and that additional criteria would be applied when appraising this medicine.

The Committee's lay member, Mr Jones, listed the patient organisations contacted by AWTTTC and noted that no submissions had been received.

The Chair invited questions or comments from the Committee. The Committee asked the company to comment on the safety profile of rufinamide in children aged less than four years, with specific reference to pneumonia and a decrease in QTc interval. The company confirmed that the clinical study showed a slightly higher percentage of pneumonia cases in patients receiving rufinamide aged between one and less than four years compared with older patients. The small number of patients included in the study of patients aged one to less than four years was noted. With regards to QTc interval shortening, the company referred to the SPC, and noted that clinical judgement should be used for prescribing rufinamide to patients at risk from further QTc shortening. The company was not aware of a higher rate of sudden deaths in this age group as a result of QTc shortening. The company highlighted that the EMA concluded the safety profile of Rufinamide in patients 1 year of age to less than 4 years of age revealed no new safety concern compared to the known safety profile in older children, adolescents and adult.

The Committee noted that rufinamide would be prescribed under specialist recommendation; arrangements for prescribing and monitoring in primary care was discussed.

Before concluding the appraisal the Chair sought confirmation from the company delegates that the appraisal process had been fair and transparent. The Chair closed the appraisal and confirmed that members would retire to vote in private.

The Chair announced the appraisal recommendation.

Appraisal decision subsequently announced in public:

The Chair 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:

Rufinamide (Inovelon®) is recommended as an option for restricted use within NHS Wales.

Rufinamide (Inovelon®) is licensed as adjunctive therapy in the treatment of seizures associated with Lennox-Gastaut syndrome in patients 1 years of age and older.

Rufinamide (Inovelon®) is restricted for use where other adjunctive treatments have proved sub-optimal or have not been tolerated.

Rufinamide (Inovelon®) is not recommended for use within NHS Wales outside of this subpopulation.

The Chair announced that confirmation of AWMSG's recommendations would be forwarded within five working days to the applicant company, who have up to ten working days to accept the recommendation or lodge a request for an independent review. It was noted that failure to respond within the deadline would not delay the process.

7. Appraisal 2: Limited Submission

Eslicarbazepine acetate (Zebinix®) adjunctive therapy in adolescents and children aged above 6 years, with partial-onset seizures with or without secondary generalisation.

The delegates from Eisai Ltd remained seated for this appraisal.

The Chair invited members to declare any interests in either the applicant company or the medicine if they had not already done so. No interests were declared.

The Chair announced 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 appraisal lead set the context of the appraisal and relayed the key aspects of the submission as outlined in the ASAR. It was confirmed that a limited submission had been considered appropriate as this was a minor licence extension. The lead highlighted that the submission had been restricted to use in the treatment of highly refractory patients who remain uncontrolled with, or are intolerant to, other anti-epileptic medicine combinations, in line with AWMSG's recommendation for adults. It was noted that the clinical efficacy data and safety profile were overall consistent with that seen in adults. The appraisal lead highlighted the limitations to the company's budget impact calculations and the potential over-estimate of the budget impact. Members were informed that the SPC had been recently updated and asked the company delegates to provide more detail.

The NMG Chair confirmed that NMG supported the restricted use of this medicine in NHS Wales for the indication stated. NMG restricted the recommendation to treatment of highly refractory patients who remain uncontrolled with, or are intolerant to, other anti-epileptic medicine combinations.

The Committee's lay member, Mr Jones, listed the patient organisations contacted by AWTTTC and noted that no submissions had been received.

The Chair opened the discussion and asked the company delegates about the recent updates to the SPC. Members were informed that a bioequivalence study had been submitted to the EMA and based on these data, the SPC has been updated to say that patients can switch from one formulation to the other. Long-term 5-year data had also been submitted to the EMA. The SPC had been updated to say that the long-term data were consistent with the known safety profile of eslicarbazepine acetate. The company confirmed that the long-term study was open-label and uncontrolled.

The Chair offered the company representatives an opportunity to address the group. There were no outstanding issues and after receiving confirmation that the appraisal process had been fair and transparent, the Chair closed the appraisal and confirmed that members would retire to vote in private.

Appraisal decision subsequently announced in public:

The Chair 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:

Eslicarbazepine acetate (Zebinix®) is recommended as an option for restricted use

within NHS Wales.

Eslicarbazepine acetate (Zebinix®) should be restricted to treatment of highly refractory patients who remain uncontrolled with, or are intolerant to, other anti-epileptic medicine combinations, within its licensed indication as adjunctive therapy in adults, adolescents and children aged above six years, with partial-onset seizures, with or without secondary generalisation.

Eslicarbazepine acetate (Zebinix®) is not recommended for use within NHS Wales outside of this subpopulation.

The Chair announced that confirmation of AWMSG's recommendations would be forwarded within five working days to the applicant company, who have up to ten working days to accept the recommendation or lodge a request for an independent review. It was noted that failure to respond within the deadline would not delay the process.

The appraisal proceedings closed.

8. AWMSG appraisal process for medicines for rare disease

Ms Sabrina Rind asked AWMSG to consider the updates to AWMSG's appraisal process for medicines for rare diseases. Ms Rind gave an overview of the updates which include simpler definitions of orphan and ultra-orphan medicines, an amendment to the process enabling a CAPIG meeting to be held if there is a positive recommendation from NMG followed by a negative recommendation from AWMSG, and aligning the cost-effectiveness thresholds to those of NICE HST interim process. Ms Rind welcomed comments and questions from the Committee.

The Committee noted that NICE's HST process is interim and asked whether AWMSG's policy would require further change. Ms Rind confirmed that AWTTTC would review the AWMSG policy in light of future changes in NICE HST methodology ensuring that the processes remained aligned. The Committee sought clarification on the weighting applied to the ICER threshold. Ms Rind and Prof Dyfrig Hughes explained how the weighing is calculated and applied. The Chair confirmed AWMSG's approval of the changes and closed discussion.

The Chair confirmed the date of the next meeting on Wednesday, 17 July 2019 in Cardiff