Enclosure No:	**1/AWMSG/0220**
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, 11th December 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 Ceri Phillips	Chair	
2.	Prof Iolo Doull	WHSSC	
3.	Prof Stephen Monaghan	Consultant in Public Health Medicine	
4.	Dr Jeremy Black	General Practitioner	
5.	Mr Hywel Pullen	Director of Finance	
6.	Mr Cliff Jones	Lay Member	
7.	Mrs Alison Hughes	Primary Care Pharmacist	
8.	Mr Tommy Price	ABPI Cymru Wales	
9.	Prof Dyfrig Hughes	Health Economist	
10.	Mrs Louise Williams	Senior Nurse	
11.	Mr Stefan Fec	Community Pharmacist	
12.	Mr John Terry	Managed Sector Secondary Care Pharmacist	

AWTTC staff in attendance:
Dr James Coulson, Interim Clinical Director & NMG Chai
Mrs Ruth Lang, Senior Liaison Manager
Ms Kath Haines, Head of WAPSU
Mr Tony Williams, Senior Appraisal Pharmacist - Team Leader
Mr Richard Boldero, Pharmacist
Dr Stephanie Francis, Senior Scientist
Dr Stuart Keeping, Senior 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
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
HEIW	Health Education and Improvement Wales
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
SPIRA	Server for Prescribing Information Reporting and Analysis
TDAPG	Therapeutic Development Appraisal Partnership Group
T&FG	Task and Finish Group
UHB	University Health Board
WAPSU	Welsh Analytical Prescribing Support Unit
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. Professor Phillips confirmed that the two appraisals would be conducted in private to protect commercial confidentiality.

2. Apologies

Dr Balwinder Bajaj, Clinical Pharmacologist
Professor Arpan Guha, Medical Director
Mr Stuart Davies (Mr Hywel Pullen attending)
Dr Cath Bale, Hospital Consultant

Mrs Cathy Wynne, Other professions eligible to prescribe

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 held on 13th November 2019 were checked for accuracy and approved.

5. Chairman's report (verbal update)

The Chair confirmed Welsh Government ratification of AWMSG's recommendations announced at the meeting held in November had been received. It was confirmed that the applicant companies had been informed and the advice had been disseminated to the service and published on the AWMSG website:

Cefepime (Renapime®) is recommended as an option for restricted use within NHS Wales.
Cefepime (Renapime®) is licensed for the treatment of infections caused by bacteria that are cefepime-sensitive: lower respiratory tract infections, including nosocomial pneumonia and community acquired pneumonia, acute bacterial exacerbation of chronic bronchitis and secondary bacterial infection of acute bronchitis; uncomplicated and complicated urinary tract infections, including pyelonephritis; skin and subcutaneous infections; intra-abdominal infections, including peritonitis and biliary tract infections; gynaecological infections; bacterial meningitis in infants and children; in combination with other antibacterial agents in the management of neutropenic patients with fever that is suspected to be due to a bacterial infection; treatment of patients with bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above. Consideration should be given to official guidance on the appropriate use of antibacterial agents.
Cefepime (Renapime®) is restricted for use for resistant pseudomonas infections where first-line agents are not effective or contraindicated.
Cefepime (Renapime®) is not recommended for use within NHS Wales outside of this subpopulation.

Diamorphine hydrochloride (Ayendi®) is recommended as an option for use within NHS Wales for the treatment of acute severe nociceptive pain in children and adolescents 2 to 15 years of age in a hospital setting. Ayendi® nasal spray should be administered in the emergency setting by practitioners experienced in the administration of opioids in children and with the appropriate monitoring.

Dupilumab (Dupixent®) is recommended as an option for restricted use within NHS Wales.
Dupilumab (Dupixent®) is licensed for the treatment of moderate-to-severe atopic dermatitis in adolescents ≥ 12 to < 18 years who are candidates for systemic therapy.
Dupilumab (Dupixent®) is restricted for the treatment of moderate-to-severe atopic dermatitis in adolescents ≥ 12 to < 18 years who are candidates for systemic therapy, only if the disease has not responded to at least one other systemic therapy, or these are contraindicated or not tolerated. Dupilumab (Dupixent®) is not recommended for use within NHS Wales outside of this subpopulation. 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.

Melatonin (Slenyto®) is not recommended for use within NHS Wales for the treatment of insomnia in children and adolescents aged 2 to 18 years with autism spectrum disorder and/or Smith-Magenis syndrome, where sleep hygiene measures have been insufficient.
The case for cost-effectiveness has not been proven.

The Chair informed members that in the absence of a submission from the holder of the marketing authorisation, a number of statements of advice had been ratified by Welsh Government and published on the AWMSG website. It was noted that these medicines for the indication specified cannot be endorsed for use within NHS Wales and should not be prescribed routinely within NHS Wales:

Ramucirumab (Cyramza®) (AWTTC Ref 2141) as monotherapy for the treatment of adult patients with advanced hepatocellular carcinoma with a baseline alpha-fetoprotein 400 ng/mL after prior sorafenib therapy

Talazoparib (Talzenna®) (AWTTC Ref 2451) as monotherapy for the treatment of adult patients with germline BRCA1 or 2 mutations, who have HER2-negative locally advanced or metastatic breast cancer. Patients should have been previously treated with an anthracycline and/or a taxane in the (neo) adjuvant, locally advanced or metastatic setting unless patients were not suitable for these treatments. Patients with hormone receptor-positive breast cancer should have been treated with a prior endocrine-based therapy, or be considered unsuitable for endocrine-based therapy

The Chair announced the next meeting would be held on Tuesday, 11th February 2020 at the Copthorne Hotel, Cardiff and he confirmed the appraisals scheduled:

Full Submission (WPAS)
Dolutegravir/lamivudine (Dovato®) for the treatment of Human Immunodeficiency Virus type 1 (HIV-1) infection in adults and adolescents above 12 years of age weighing at least 40 kg, with no known or suspected resistance to the integrase inhibitor class, or lamivudine
Applicant company: ViiV Healthcare UK Ltd

Full Submission
Plerixafor (Mozobil®) in combination with granulocyte-colony stimulating factor (G-CSF) to enhance mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in children aged 1 to less than 18 years with lymphoma or solid malignant tumours, either: pre-emptively, when circulating stem cell count on the predicted day of collection after adequate mobilization with G-CSF (with or without chemotherapy) is expected to be insufficient with regards to desired hematopoietic stem cells yield; or who previously failed to collect sufficient haematopoietic stem cells
Applicant company: Sanofi

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 or contact Ruth Lang at AWTTC for further information on the appraisal process and future work programme.

The Chair reminded members that the Annual AWMSG Training Day would be held in Cardiff City Stadium on Wednesday, 15th January 2020. He confirmed the theme of the day would be the future vision of AWMSG. He encouraged all members to attend.

6. National Prescribing Indicators 2019-20 - Analysis of Prescribing Data to June 2019

Mr Boldero presented an overview of the prescribing data to June 2019 and drew members' attention to areas of good and poor prescribing. The Chair opened discussion. Mr Boldero confirmed that the purpose of the Prescribing Safety Indicators was to support direct intervention and review of patients at practice level. Variations in prescribing were highlighted and members agreed that feedback following review of patients would be useful in explaining the variations. Ms Haines reminded members that the medicines safety dashboard on SPIRA enabled further exploration of the data. It was confirmed that the Prescribing Safety Indicators are being monitored as part of Welsh Government's Quality Assurance and Improvement Framework (QAIF). One member suggested that the capturing of real-world safety outcome

data at the same time would be valuable. There was acknowledgement that increased engagement with health boards would be helpful. The Chair confirmed he would be writing to Health Board Chief Executives and Chief Pharmacists after the meeting asking for a response to the data in the report as there were areas of performance that required further exploration.

ACTION

Chair to write to Health Board Chief Executives and Chief Pharmacists

7. Feedback from the AWPAG meeting held 18th September 2019

Ms Haines presented an overview of the draft minutes of the AWPAG meeting held on 18th September 2019. She highlighted work currently on-going and confirmed a further meeting had been held on 11th December. Ms Haines informed members that the Respiratory Health Implementation Group were developing guidelines and these would be presented to AWMSG following consultation. There was discussion in relation to the value of developing guidelines specific for Wales - some members expressed a view that variation in guidance is unwarranted. The point was made that NICE guidance is specific to NHS England and the availability of all-Wales consensus guidelines, endorsed by AWMSG, might be useful in some circumstances. Members acknowledged the importance of clinical and patient choice. The Chair reminded members that accepted clinical practice provided validity to guidance and divergence from NICE guidance may be accepted in Wales provided the reasons for the divergence had been clearly understood and documented. The Chair confirmed that due process and consultation during the development of guidance would also be taken into account by AWMSG when considering endorsement.

8. Identifying and delivering the key priorities for AWMSG

The Chair presented Enc 4 and explained that the context behind the discussion document was the remit letter he had received from the Health Minister and the alignment with goals of 'A Healthier Wales'. The Chair stated the purpose of the document was to stimulate discussion and encourage AWMSG members to be proactive in contributing to AWMSG's strategic work programme. The Chair asked members to liaise with their constitutent organisations and provide a response to AWTTC by 10th January 2020. It was confirmed that Welsh Government's definition of value-based healthcare would be emailed to members outside of the meeting to provide clarity. Members welcomed the opportunity to respond and improve engagement. The Chair confirmed that AWMSG needs to drive the agenda on medicines management in Wales.

ACTION

All members to respond to the Chair by 10th January 2020

AWTTC to email Welsh Government's definition of value-based healthcare to members

"To improve the health outcomes of the people in Wales, in a financially sustainable way, through the creation of a data-driven system, which seeks to provide timely information to citizens, clinical teams and organisations to inform decision-making".

The Chair moved to agenda item 11 as the meeting would be closed to the public for the appraisal sessions.

11. Any other business

Mrs Lang informed members of an NHS England Consultation on the 'NHS Commercial Framework for Medicines' which was published in November 2019. The deadline for responding is 10th January 2020.

Members were informed that the NICE Public Board Meeting and Question Time will be held at the All Nations Centre on Wednesday, 29th January 2020. The question time session will run from 12.30 pm to 1.15 pm and the Public Board Meeting will commence at 1.30 pm to 4.00 pm. Registration is required if members wish to attend.

Nominations were invited for membership to the Welsh NICE Health Network. Mrs Lang confirmed that draft terms of reference for the Network would be circulated to members after the meeting.

ACTION

AWTTC to email draft terms of reference of the Welsh NICE Health Network

The meeting closed to the public and individuals in the public gallery left the meeting. The Chair sought confirmation that the individuals remaining in the public gallery were affiliated to either AWTTC or the applicant company. A representative from the patient organisation Metabolic Support UK made herself known to the Chair. The company delegates from Immedica Pharma confirmed that they were happy for this individual to observe the appraisal.

9. Appraisal 1: Full Submission (WPAS)

Glycerol phenylbutyrate (Ravicti®) adjunctive therapy for chronic management of patients with urea cycle disorders including deficiencies of carbamoyl phosphate-synthase-I (CPS), ornithine carbamoyltransferase (OTC), argininosuccinate synthetase (ASS), argininosuccinate lyase (ASL), arginase I (ARG) and ornithine translocase deficiency hyperornithinaemia-hyperammonaemia homocitrullinuria syndrome (HHH) who cannot be managed by dietary protein restriction and/or amino acid supplementation alone. Ravicti must be used with dietary protein restriction and, in some cases, dietary supplements (e.g. essential amino acids, arginine, citrulline, protein-free calorie supplements)

The Chair welcomed the delegates from Immedica Pharma.

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 and outlined the sequence of events. Members were reminded that NMG had considered the clinical and cost effectiveness issues in detail and there was no expectation that AWMSG would repeat this. The Chair encouraged members to seek clarification of any outstanding issues, particularly in relation to budget impact, and to take into consideration any societal aspects that were not part of the discussion at NMG. The Chair confirmed that delegates from the applicant company would have the opportunity to respond to questions and highlight any salient issues with regard to their submission. The Chair handed over to the AWTTC appraisal lead.

The AWTTC appraisal lead presented an overview and relayed the key aspects of the submission as outlined in the ASAR.

The Chair invited Dr James Coulson to relay the recommendation of the NMG. Dr Coulson confirmed the positive advice of NMG following appraisal of glycerol phenylbutyrate (Ravicti®) on 6th November as detailed in the PAR. Dr Coulson confirmed that NMG had agreed that glycerol phenylbutyrate (Ravicti®) was considered to be a medicine for a rare disease and broader considerations had been taken into account utilising the AWMSG orphan/ultra orphan/rare disease policy. Dr Coulson relayed the advantages of the medicine that had been highlighted by the clinical expert at the NMG meeting.

The Chair opened discussion in relation to clinical effectiveness and members sought clarification of aspects of the study design and clinical trial evidence. Clarification relating to bottle size, shelf life and syringe availability was additionally sought from the company

delegates.

Professor Hughes summarised the case for cost effectiveness and the Chair referred members to the budget impact estimates. The company explained their reasons for submitting a cost minimisation analysis rather than a cost-utility analysis.

The Chair reminded members of the importance of considering the wider societal issues and the advantages of a licensed medicine with improved palatability were noted. The company delegates highlighted the benefit of treatment away from the home setting and the potential for reduced stress on carers and family members. The lay member summarised the views submitted by the patient organisation, Metabolic Support UK.

Having received confirmation from the company delegates that the appraisal process had been fair and transparent, the Chair closed the appraisal and members retired 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:

Glycerol phenylbutyrate (Ravicti®) is recommended as an option for use within NHS Wales for use as an adjunctive therapy for chronic management of patients with urea cycle disorders including deficiencies of: carbamoyl phosphate synthetase I (CPS); ornithine carbamoyltransferase (OTC); argininosuccinate synthetase (ASS); argininosuccinate lyase (ASL); arginase I (ARG) and ornithine translocase deficiency hyperornithinaemia-hyperammonaemia homocitrullinuria syndrome (HHH) who cannot be managed by dietary protein restriction and/or amino acid supplementation alone. Ravicti® must be used with dietary protein restriction and, in some cases, dietary supplements (for example, essential amino acids, arginine, citrulline, protein-free calorie supplements). This recommendation applies only in circumstances where the approved Wales Patient Access Scheme (WPAS) is utilised or where the list/contract price is equivalent or lower than the PAS/WPAS price.

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.

10. Appraisal 2: Full Submission (WPAS)
Fampridine (Fampyra®) for the improvement of walking in adult patients with multiple sclerosis with walking disability (EDSS 4–7)

The Chair welcomed delegates from Biogen Idec Limited

The Chair sought confirmation that the individuals remaining in the public gallery were affiliated to either AWTTC or the applicant company.

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 and

outlined the sequence of events. Members were reminded that NMG had considered the clinical and cost effectiveness issues in detail and there was no expectation that AWMSG would repeat this. The Chair encouraged members to seek clarification of any outstanding issues, particularly in relation to budget impact, and to take into consideration any societal aspects that were not part of the discussion at NMG. The Chair confirmed that delegates from the applicant company would have the opportunity to respond to questions and highlight any salient issues with regard to their submission. The Chair handed over to the AWTTC appraisal lead.

The AWTTC appraisal lead presented an overview and relayed the key aspects of the submission as outlined in the ASAR.

The Chair invited Dr James Coulson to relay the recommendation of the NMG. Dr Coulson confirmed the positive advice of NMG following appraisal of fampridine (Fampyra®) on 6th November. Dr Coulson highlighted key aspects of the submission that led to positive advice being issued by NMG to AWMSG as detailed in the PAR.

The Chair opened discussion in relation to clinical effectiveness. The unmet clinical need was noted. Members sought clarification of the evidence of effectiveness and questioned whether it was clinically significant. The difficulties in capturing quality of life data were acknowledged and members noted that benefits went beyond those captured using the standard methods. Clarification was sought in relation to the NICE guideline186 published July 2019. The company delegates confirmed that the guideline was currently being reviewed by NICE.

Professor Hughes summarised the case for cost effectiveness. He clarified the thresholds for cost-effectiveness and the impact of wider benefits. The Chair referred members to the budget impact estimates.

The lay member summarised the views received from the MS Society and three individual patients. The summary included comprehensive reference to a number of functional benefits and highlighted the potential to transform the lives of people suffering with MS and improve family life.

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.

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:

Fampridine (Fampyra®) is recommended as an option for use within NHS Wales for the improvement of walking in adult patients with multiple sclerosis with walking disability (Expanded Disability Status Scale [EDSS] 4 to 7). This recommendation applies only in circumstances where the approved Wales Patient Access Scheme (WPAS) is utilised or where the list/contract price is equivalent or lower than the WPAS price.

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 meeting closed.

Date of the next meeting - Tuesday, 11th February 2020 in Cardiff