Enclosure No:	**1/AWMSG/0716**
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, 15th June 2016 commencing 9.30 am at the Park Inn Hotel Cardiff North, Circle Way East, Llanedeyrn, Cardiff CF23 9XF

VOTING MEMBERS PRESENT:

Did not participate in

1.	Dr Stuart Linton	Chair
2.	Prof John Watkins	Public Health Wales
3.	Dr Jeremy Black	General Practitioner
4.	Dr Karen Fitzgerald	Consultant in Pharmaceutical Public Health
5.	Prof Dyfrig Hughes	Health Economist
6.	Dr Sian Lewis	Welsh Health Specialised Services Committee
7.	Mrs Alison Hughes	Managed Sector Primary Care Pharmacist
8.	Mr Chris Palmer	Lay Member
9.	Mr Bill Malcolm	ABPI Cymru Wales
10.	Mr Stuart Davies	Finance Director
11.	Dr Mark Walker	Medical Director
12.	Mrs Louise Williams	Senior Nurse
13.	Mr John Terry	Managed Sector Secondary Care Pharmacist

WELSH GOVERNMENT:
No representation

IN ATTENDANCE:
Dr Saad Al-Ismail, NMG Chair
Mrs Karen Samuels, Head of Patient Access, AWTTC
Mrs Ruth Lang, Head of Liaison & Administration, AWTTC

AWTTC APPRAISAL LEADS:
Mrs Helen Adams, Senior Appraisal Pharmacist
Dr Caron Jones, Senior Appraisal Scientist
Dr Stephanie Francis, 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
CAPIG	Clinical and Patient Involvement Group
CEPP	Clinical Effectiveness Prescribing Programme
CHMP	Committee for Medicinal Products for Human Use
DoH	Department of Health
ECDF	English Cancer Drugs Fund
EMA	European Medicines Agency
EOL	End of life
FAR	Final Appraisal Recommendation
FDA	US Food and Drug Administration
GP	General Practitioner
HAC	High Acquisition Cost
HB	Health Boards
HST	Highly Specialised Technology
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 Care Excellence
NMG	New Medicines Group
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 Chairman opened the meeting and welcomed members.

2. Apologies

Dr Cath Bale and Dr Sue Jeffs representing Hospital Consultants
Mr Scott Cawley representing 'other professions eligible to prescribe'
Mrs Ellen Lanham and Mr Stefan Fec representing Community Pharmacists
Dr Emma Mason, Clinical Pharmacologist representative

3. Declarations of interest

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

4. Minutes of previous meeting

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

5. Chairman's Report

The Chairman confirmed receipt of ministerial ratification in relation to the following recommendations:

Dulaglutide (Trulicity®) is recommended as an option for restricted use within NHS Wales. Dulaglutide (Trulicity®) should be restricted for use in the following subpopulation/circumstances within its licensed indication for the treatment of type 2 diabetes in adults to improve glycaemic control:

- After failure, intolerance or where there is a contraindication to, standard triple therapy (metformin and two other antidiabetic medicines) as an alternative to insulin therapy.

- In combination with other glucose-lowering medicinal products but not including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control, in line with current NICE guidance.

Dulaglutide (Trulicity®) is not recommended for use within NHS Wales outside of this subpopulation/these circumstances.

Pasireotide (as pamoate) (Signifor®) is recommended as an option for use within NHS Wales for the treatment of adult patients with acromegaly for whom surgery is not an option or has not been curative and who are inadequately controlled on treatment with another somatostatin analogue.

The Chairman reported that final NICE Highly Specialised Technology (HST) advice in relation to ataluren (Translarna®) for treating children aged 5 and over with Duchenne muscular dystrophy (DMD) caused by a nonsense mutation is anticipated in July 2016. Members were informed that Welsh Health Specialised Services Committee foresaw no barriers to implementation of the advice within NHS Wales should it be positively recommended by NICE. The Chairman confirmed that on this basis, and in order to provide timely advice to Welsh Government, Welsh Government will be advised to implement the NICE HST advice.

The Chairman confirmed receipt of ministerial ratification in relation to the following statements of advice and reiterated that in the absence of a submission the medicines could not be endorsed for use within NHS Wales and routinely funded.

Carfilzomib (Kyprolis®) in combination with lenalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy

Ferric maltol (Feraccru®) cannot be endorsed for use within NHS Wales for the treatment of iron deficiency anaemia in adults with inflammatory bowel disease

Ibrutinib (Imbruvica®) for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) who have received at least one prior therapy, or in first line in the presence of 17p deletion or TP53 mutation in patients unsuitable for chemo-immunotherapy
Ibrutinib (Imbruvica®) for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL)

The Chairman announced the appraisals are scheduled for the next AWMSG meeting to be held on Wednesday, 13th July 2016 in Cardiff Metropolitan University:

Appraisal 1: Full Submission
Ceftolozane/tazobactam (Zerbaxa®) for the treatment of the following infections in adults: complicated intra-abdominal infections; acute pyelonephritis; complicated urinary tract infections. Consideration should be given to official guidance on the appropriate use of antibacterial agents
Applicant Company: Merck Sharp & Dohme Ltd

Appraisal 2: Limited Submission
Aprepitant (EMEND®) for the prevention of nausea and vomiting associated with highly and moderately emetogenic cancer chemotherapy in patients from the age of 6 months to less than 18 years old. Aprepitant is given as part of combination therapy
Applicant Company: Merck Sharp & Dohme Ltd

Appraisal 3: Full Submission (WPAS) (Orphan/Ultra-orphan)
Blinatumomab (Blincyto®) for the treatment of adults with Philadelphia chromosome negative relapsed or refractory B-precursor acute lymphoblastic leukaemia
Applicant Company: Amgen Ltd

Appraisal 4: Full Submission (WPAS)
Netupitant/palonosetron (Akynzeo®) in adults for the prevention of acute and delayed nausea and vomiting associated with highly emetogenic cisplatin‑based cancer chemotherapy and for the prevention of acute and delayed nausea and vomiting associated with moderately emetogenic cancer chemotherapy
Applicant Company: Chugai Pharma UK Ltd

Appraisal 5: Full Submission (WPAS)
Lenalidomide (Revlimid®) for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant
Applicant Company: Celgene Ltd

Appraisal 6: Limited Submission (WPAS)
Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (Genvoya®) for the treatment of adults and adolescents (aged 12 years and older with body weight at least 35 kg) infected with human immunodeficiency virus 1 (HIV-1) without any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir
Applicant Company: Gilead Sciences Ltd

The Chairman confirmed that four of the six appraisals would be held in private because of the commercial sensitivity of the patient access scheme. The meeting will be closed to the public after the second appraisal.

Members were reminded to declare any interests in relation to these appraisals before the next meeting. Patients, patient organisations and patient carers were invited to submit their views to AWTTC in relation to medicines scheduled for appraisal. The Chairman reminded members to sign and return the confidentiality statements to AWTTC.

6. Appraisal 1: Full Submission

Misoprostol (Mysodelle®) for induction of labour in women with an unfavourable cervix, from 36 weeks gestation, in whom induction is clinically indicated

The Chairman welcomed representation from Ferring Pharmaceuticals 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 interests were declared.

The Chairman 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 Chairman outlined the sequence of events and invited the AWTTC Appraisal Lead to set the context of the appraisal.

Mrs Adams highlighted the key aspects of the submission outlined in the ASAR. The Chairman invited Dr Al-Ismail to feedback the relevant issues identified in the preliminary appraisal. Dr Al-Ismail confirmed that NMG had appraised misoprostol (Mysodelle®) on 11th May 2016 and did not recommend it for use within NHS Wales for the induction of labour in women with an unfavourable cervix, from 36 weeks gestation, in whom induction is clinically indicated. NMG considered that the case for cost-effectiveness had not been proven. Dr Al-Ismail stated that NMG were not convinced that the evidence presented was sufficient to demonstrate therapeutic equivalence between misoprostol (Mysodelle®) and the comparator. Therefore, the evidence to justify the cost minimisation analysis presented in the submission was insufficient for NMG to recommend its use.

The Chairman opened the discussion in relation to clinical effectiveness. Clarification was sought in relation to the adverse effects. The applicant company highlighted that the adverse events profile was consistent with that expected given the differences in mechanism of action between the two medicines. Members discussed the need for patient choice in relation to duration of labour and intensity of contractions/pain. There was discussion in relation to patient satisfaction and it was confirmed by the applicant company that this had not been included in the pivotal study. The applicant company highlighted that there is evidence to suggest that reduced time to delivery is a perceived unmet need by women undergoing induction of labour. They stated that they intend to collect data on patient satisfaction in countries where Mysodelle® is already being used. Members expressed concern over the transferability of results from a study conducted in the United States to the clinical setting in Wales. In addition clarification was sought in relation to use of such medicines in an outpatient setting. The potential for reduction in hospital stay was noted. The Chairman referred members to the summary of clinical expert views and Mrs Adams highlighted that misoprostol would offer clinicians an alternative treatment option. Clinical experts stated a wider unmet need in relation to the induction of labour in general, although no specific unmet need in relation to Mysodelle® was highlighted. Experts had concerns in relation to increased risk of uterine hyperstimulation and the potential implication on resources.

The Chairman invited Professor Hughes to comment on the case for cost-effectiveness. Professor Hughes confirmed his role as AWMSG health economist. Professor Hughes summarised the case presented as outlined in the ASAR and highlighted the key issues. He stated that in his view a cost minimisation analysis (CMA) was not appropriate as therapeutic equivalence had not been demonstrated across all health outcomes. It was noted that the demonstrated difference in hospital stay is statistically significant and that differences were also highlighted in adverse events and potentially in patient preference. The company delegates responded and explained their rationale for presenting a CMA and suggested any differences in QALY would be very small. Members went on to consider and comment on the budget impact estimates. A member expressed concern that calculation of costs in the US hospital setting is

not the same as that for the UK. Mrs Samuels confirmed that a cost utility analysis had been requested.

The Chairman highlighted the role of the lay member in ensuring that patient, carer and public views and experiences inform AWMSG. He referred members to the patient organisation questionnaire from the Birth Trauma Association and confirmed that all members had received and read the documentation. For the purposes of transparency the Chairman asked Mr Palmer to summarise the issues. Mr Palmer highlighted the potential for psychological trauma associated with fast onset of labour and delivery and the adverse effects associated with the treatment. The Chair asked members to highlight any outstanding societal issues. The applicant company reiterated the need for patient choice highlighting the adverse events which can be associated with a prolonged labour. They also confirmed Mysodelle® is already available elsewhere in the UK.

The Chairman referred to the applicant company's response and offered further opportunity for the company delegates to comment prior to concluding the appraisal. The company delegate suggested to members that a precedent had been set in accepting a cost minimisation analysis. Having received confirmation that the appraisal process had been fair and transparent and that all relevant issues had been discussed, the Chairman closed the appraisal.

Appraisal decision subsequently announced in public:
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:

Misoprostol (Mysodelle®) is not recommended for use within NHS Wales for the induction of labour in women with an unfavourable cervix, from 36 weeks gestation, in whom induction is clinically indicated. The case for cost-effectiveness has not been proven.

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded within five working days. He informed company delegates that they had 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.

8. Appraisal 2: Full Submission

Olanzapine (ZypAdhera®) for the maintenance treatment of adult patients with schizophrenia sufficiently stabilised during acute treatment with oral olanzapine

The Chairman welcomed representation from Eli Lilly and Co 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 interests were declared.

The Chairman alluded 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, 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 outlined the sequence of events and invited the AWTTC Appraisal Lead to set the context of the appraisal.

Dr Jones highlighted the key aspects of the submission outlined in the ASAR and confirmed that the applicant company had made a resubmission based on a sub-population where they perceived maximum benefit of treatment. The Chairman invited Dr Al-Ismail to feedback the relevant issues identified in the preliminary appraisal. Dr Al-Ismail confirmed that NMG had appraised olanzapine (ZypAdhera®) and did not recommend it for use within NHS Wales for the

maintenance treatment of adult patients with schizophrenia sufficiently stabilised during acute treatment with oral olanzapine as the case for cost-effectiveness had not been proven. Dr Al-Ismail informed members that NMG was not convinced that the evidence presented was sufficient to demonstrate therapeutic equivalence between olanzapine (ZypAdhera®) and the comparator. Therefore, the evidence to justify the cost minimisation analysis presented in the submission was insufficient for NMG to recommend its use.

The Chairman opened discussion in relation to clinical effectiveness. Members asked for clarification of the specific patient population and the company delegate explained that its use should be limited for use only in responders to oral olanzapine who had failed all other antipsychotic treatment and were non-adherent. It was clearly explained to members that in the absence of this medicine, patients would have no other treatment options. There was discussion over the three hour observation period post treatment, and the company delegate went to great lengths to explain that this did not involve any monitoring; it was purely observation of the behaviour to ensure that the patient did not experience post-injection syndrome, and could be undertaken by a healthcare support staff. The company delegate explained that the key issue with this patient population is compliance and the mechanism to ensure compliance was acknowledged by members.

Dr Jones relayed the views of clinical experts and members acknowledged the variability in relation to psychological treatment across NHS Wales. Experts highlighted the importance of tolerability and compliance, and considered that there is an unmet need in this small niche patient population.

The Chairman invited Professor Hughes to comment on the case for cost-effectiveness. Professor Hughes confirmed his role as AWMSG health economist. Professor Hughes summarised the case presented as outlined in the ASAR. He highlighted the limitations in the case for cost-effectiveness, as presented in the applicant company's submission. Members were also mindful of the key factors influencing the recommendation made by NMG. Mrs Samuels confirmed that a cost utility analysis had been requested. The company delegate responded to the comments and acknowledged that it was unusual to compare a medicine against no treatment. He stated that it was a complex issue and there were challenges in providing a case for cost-effectiveness. He alluded to data from Sweden which demonstrated clear and real-world outcomes which were relevant to NHS Wales. Discussion moved to the budget impact and the very small suggested sub-set of the patient population was noted. Members were mindful that access via the individual patient funding request process would be unlikely to be considered appropriate for the majority of these patients.

The Chairman highlighted the role of the lay member in ensuring that patient, carer and public views and experiences inform AWMSG. He referred members to the patient organisation questionnaire from Hafal and confirmed that all members had received and read the documentation. For the purposes of transparency the Chairman asked Mr Palmer to highlight the salient aspects of the patient questionnaire. The organisation highlighted that the medicine would offer an alternative for a very small number of patients with very limited treatment options. Members considered societal issues and acknowledged that carers would need to accept the inconvenience of the post-treatment observation and understand the benefit to the patient. Members noted the value of the social component to a non-compliant patient in receiving regular communication and treatment. The company delegate highlighted mandatory online training for prescribers and explained that the medicine would not be supplied if the appropriate training had not been undertaken. The issue of discontinuation of therapy and relapse was raised, and the delegate informed members that examples of treatment and monitoring protocols from Centres based in England were available on the company's website.

The Chairman referred to the applicant company's response and offered further opportunity for the company delegates to comment prior to concluding the appraisal. Having received confirmation that the appraisal process had been fair and transparent and that all relevant issues had been discussed, the Chairman closed the appraisal.

Appraisal decision subsequently announced in public:
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:

Olanzapine (ZypAdhera®) is recommended as an option for restricted use within NHS Wales.

Olanzapine (ZypAdhera®) is licensed for the maintenance treatment of adult patients with schizophrenia sufficiently stabilised during acute treatment with oral olanzapine.

Olanzapine (ZypAdhera®) is restricted for use in a subpopulation of patients more appropriately managed with a long acting injection formulation because of difficulties adhering to an oral olanzapine regimen, indicated by recurrent relapse or exacerbation of symptoms

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

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded within five working days. He informed company delegates that they had 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 was closed to members of the public.

11. Appraisal 3: Limited Submission (PAS)
Evolocumab (Repatha®) for the treatment in adults and adolescents aged 12 years and over with homozygous familial hypercholesterolaemia in combination with other lipid-lowering therapies

The Chairman welcomed representation from Amgen UK & Ireland and confirmed that individuals remaining in the public gallery were AWTTC staff. The Chairman confirmed that the recommendation of AWMSG following appraisal of evolcoumab would not be announced in public until final NICE guidance in relation to the heterozygous hypercholesterolaemia and mixed dyslipidaemia indication is published. The Chairman confirmed that it was on this basis that AWTTC accepted a limited submission and it was noted that the Department of Health approved patient access scheme would only be applied on publication of positive NICE guidance. The Chairman confirmed his acceptance that in these unusual circumstances the appraisal by AWMSG would proceed so that advice could be available within NHS Wales at the earliest appropriate time.

The Chairman 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 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, 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 informed members that the application had been considered eligible for a limited submission and no cost-effectiveness information is required. He confirmed that the marketing authorisation holder would be expected to provide evidence of budgetary impact in comparison to the existing comparator product/s. The Chairman reiterated that monitoring of budget impact

would be essential and AWMSG reserved to right to request a full submission if the budget impact exceeded that estimated in the submission.

Dr Francis presented an overview of the submission as outlined in the ASAR. The Chairman invited Dr Al-Ismail to relay the view of NMG. Dr Al-Ismail confirmed that NMG had considered this medicine at their meeting on 11th May and supported the use of evolocumab as an option for use within NHS Wales for the treatment of adults and adolescents aged 12 years and over with homozygous familial hypercholesterolaemia in combination with other lipid-lowering therapies. Dr Al-Ismail reiteration that the recommendation should apply 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.

Dr Francis relayed the views of clinical experts that there is an unmet clinical need in terms of treatment options for these patients. The applicant company estimated that three Welsh patients would be eligible for treatment and clinical experts considered this to be a reasonable estimate. The Chairman asked members to highlight any outstanding issues. Clarification was sought in relation to the specific patient population and it was acknowledged that homozygous familial hypercholesterolaemia is extremely rare and treatment options are very limited. It was noted that the marketing authorisation holder of the alternative licensed medicine had to date not engaged in the AWMSG appraisal process.

The Chairman confirmed that no patient organisation questionnaires had been received and Mr Palmer informed members that four organisations had been approached by AWTTC.

The Chairman referred to the applicant company's response and offered further opportunity for the company delegates to comment prior to concluding the appraisal. Having received confirmation that the appraisal process had been fair and transparent and that all relevant issues had been discussed, the Chairman closed the appraisal and members retired to vote in private.

12. Date of next meeting

The Chairman confirmed the date of the next meeting on **Wednesday, 13th July 2016 in Cardiff Metropolitan University** and closed proceedings.