Enclosure No:	**1/AWMSG/1115**
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, 21st October 2015 commencing 9.30 am at the Park Inn Hotel Cardiff North, Circle Way East Cardiff CF23 9XF

VOTING MEMBERS PRESENT:

			Did not participate in
1.	Dr Stuart Linton	Chairman	
2.	Professor John Watkins	Public Health Wales / Vice Chairman	
3.	Dr Sue Jeffs	Hospital Consultant	
4.	Dr Jeremy Black	General Practitioner	
5.	Dr Geoffrey Carroll	Welsh Health Specialised Services Committee	
6.	Mr Stuart Davies	Finance Director	
7.	Professor David Cohen	Health Economist	
8.	Dr Karen Fitzgerald	Public Health Wales	
9.	Mr Stefan Fec	Community Pharmacist	
10.	Dr Emma Mason	Clinical Pharmacologist	
11.	Mr Christopher Palmer	Lay Member	
12.	Mr Robert Thomas	ABPI Cymru Wales	6, 8
13.	Mr Roger Williams	Managed Sector Secondary Care Pharmacist	9,10
14.	Mrs Louise Williams	Senior Nurse	

WELSH GOVERNMENT:
No representation at the meeting

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

AWTTC APPRAISAL LEADS:
Dr Caron Jones, Senior Appraisal Scientist
Ms Kelly Wood, Senior Appraisal Scientist
Dr Claire Davis, 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

Welcome and introduction

1. The Chairman opened the meeting and welcomed Dr Jeremy Black to his first meeting as General Practitioner representative. He confirmed that Dr Black had previously served as a member of AWPAG.

2. Apologies

Mrs Alison Hughes and Mrs Susan Murphy (Managed Sector Primary Care Pharmacist)
Mr Alun Morgan and Mr Scott Cawley (Other professions eligible to prescribe)
Dr Mark Walker and Dr Brendan Boylan (Medical Director)
Dr Catherine Bale (Dr Sue Jeffs deputising)

3. Declarations of interest

The Chairman invited declarations of interest pertinent to the agenda. Mr Rob Thomas declared an interest in Appraisal 1, insulin degludec/liraglutide (Xultophy®) and Appraisal 3 tiotropium (Spiriva® Respimat®) and the Chairman confirmed that he would not participate in these appraisals or votes.

4. Minutes of previous meeting

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

5. Chairman's report

The Chairman confirmed that the Minister for Health and Social Services had ratified AWMSG's advice from the September meeting.

Lisdexamfetamine dimesylate (Elvanse Adult®▼) is recommended as an option for use within NHS Wales as part of a comprehensive treatment programme for attention deficit/hyperactivity disorder (ADHD) in adults.

Riociguat (Adempas®▼) is recommended for use within NHS Wales for the treatment of adult patients with WHO functional class II to III with inoperable chronic thromboembolic pulmonary hypertension (CTEPH); or persistent or recurrent CTEPH after surgical treatment to improve exercise capacity. This recommendation applies only in circumstances where the approved Wales Patient Access Scheme is utilised.

Riociguat (Adempas®▼) is recommended as an option for restricted use within NHS Wales for the treatment of adult patients with pulmonary arterial hypertension (PAH) with WHO functional class II to III to improve exercise capacity. This recommendation applies only in circumstances where the approved Wales Patient Access Scheme is utilised.
Riociguat (Adempas®▼) should be restricted for use as a PAH-specific monotherapy as an alternative treatment option to endothelin receptor antagonist (ERA) monotherapy in adult patients with PAH of WHO functional class II to III.
Riociguat (Adempas®▼) is not recommended for use within NHS Wales outside of this subpopulation.

The Chairman confirmed the advice had been disseminated to health boards and uploaded to the AWMSG website.

Members were reminded of the AWMSG/NMG Training Day to be held on Wednesday, 27th January 2016 at the Cardiff City Stadium. The Chairman announced that AWMSG would be extending the invitation to IPFR panel members and Medicines & Therapeutics Committees. He asked members to complete a form identifying training requirements to make the day as productive as possible.

The Chairman announced the postponement of appraisals in relation to cetuximab (Erbitux®)for the treatment of patients with epidermal growth factor receptor (EGFR)-expressing, RAS wild-type metastatic colorectal cancer, in combination with irinotecan-based chemotherapy, in first-line in combination with FOLFOX, as a single agent in patients who have failed oxaliplatin- and irinotecan-based therapy and who are intolerant to irinotecan and ivacaftor (Kalydeco®) for the treatment of cystic fibrosis (CF) in patients age 6 years and older who have one of the following gating (class III) mutations in the CFTR gene: G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, or S549R.

The marketing authorisation holder of cetuximab (Erbitux), Merck Serono Limited, had requested a meeting to explore issues relating to AWMSG's policy for appraising medicines at the end of life.

He further informed members that following receipt of NMG's recommendation not supporting use of ivacaftor for the indication appraised, the marketing authorisation holder, Vertex Pharmaceuticals Limited, had requested a meeting of the Clinical and Patient Involvement Group (CAPIG).

The Chairman confirmed that the AWMSG Steering Committee had met on Monday, 19th October and had reconsidered AWMSG's policy regarding the appraisal of biosimilar medicines. He reiterated that the managed and timely introduction of biosimilar medicines into clinical practice in NHS Wales is desirable and, to facilitate this, AWTTC had proposed that AWMSG should no longer routinely appraise all biosimilar medicines. Where the reference product has been recommended for use by AWMSG or NICE for the same indication(s) and in the same population, or was initially licensed and available prior to 1st October 2002, and the cost of the new biosimilar medicine is equivalent to or lower than the reference medicine, AWTTC proposed that the application would normally be excluded from appraisal by AWMSG. A full submission would continue to be requested for indication(s)/populations where the reference product had been appraised by AWMSG or NICE and was not recommended for use, or in circumstances where the reference medicine had been licensed post October 2002 and had not been appraised by AWMSG or NICE. The Chairman confirmed that the proposal had been supported by the Steering Committee, and AWTTC would be updating AWMSG's Exclusion Criteria and the Frequently Asked Questions to this effect.

The Chairman announced the appraisals scheduled for the next AWMSG meeting to be held on Wednesday, 11th November 2015 in Cardiff.

Full Submissions:

Insulin glargine (Abasaglar®) for the treatment of diabetes mellitus in adults, adolescents and children aged 2 years and above
Applicant Company: Eli Lilly & Co Ltd

Sucroferric oxyhydroxide (Velphoro®) for the control of serum phosphorus levels in adult chronic kidney disease (CKD) patients on haemodialysis (HD) or peritoneal dialysis (PD). Sucroferric oxyhydroxide (Velphoro®) should be used within the context of a multiple therapeutic approach, which could include calcium supplement, 1,25-dihydroxy vitamin D3 or one of its analogues, or calcimimetics to control the development of renal bone disease
Applicant Company: Fresenius Medical Care UK Ltd

Tedizolid phosphate (Sivextro®) for the treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults
Applicant Company: Merck Sharp & Dohme Ltd

Limited submissions

Denosumab (Xgeva®) for the treatment of adults and skeletally mature adolescents with giant cell tumour of bone that is unresectable or where surgical resection is likely to result in severe morbidity
Applicant Company: Amgen Ltd

Tinzaparin sodium (Innohep®) for the extended treatment of symptomatic venous thromboembolism and prevention of its recurrence in patients with solid tumours
Applicant Company: LEO Laboratories Ltd

Raltegravir (Isentress®) in combination with other anti-retroviral medicinal products for the treatment of human immunodeficiency virus (HIV-1) infection in adults, adolescents, children, toddlers and infants from the age of 4 weeks
Applicant Company: Merck Sharp & Dohme Ltd

Adalimumab (Humira®)for the treatment of severe chronic plaque psoriasis in children and adolescents from 4 years of age who have an inadequate response to or are inappropriate candidates for topical therapy and phototherapies
Applicant Company: AbbVie Ltd

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.

6. Appraisal 1: Full Submission
Insulin degludec/liraglutide (Xultophy®) for the treatment of adults with type 2 diabetes mellitus to improve glycaemic control in combination with oral glucose-lowering medicinal products when these alone or combined with a GLP-1 receptor agonist or basal insulin do not provide adequate glycaemic control

The Chairman welcomed representation from the applicant company Novo Nordisk Ltd.

Mr Rob Thomas left the meeting. 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 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 Dr Stephanie Francis, AWTTC Appraisal Lead, to set the context of the appraisal.

Dr Francis presented an overview of the submission as detailed in the ASAR and clarified that Novo Nordisk Ltd had focused their submission on a subpopulation of the licensed indication for the use of Xultophy as an add-on therapy for patients whose glucose levels are uncontrolled on basal insulin. Members were informed that the medicine is available for restricted use following a positive HTA in Scotland. Dr Francis highlighted the key aspects of the ASAR and confirmed that Novo Nordisk do not anticipate the medicine will be supplied by a home healthcare provider. Dr Francis confirmed that three patient organisation questionnaires had

been received.

The Chairman invited Dr Saad Al-Ismail, the NMG Chairman, to provide a brief overview of the relevant issues identified in the preliminary appraisal. Dr Al-Ismail confirmed the view of NMG that insulin degludec/liraglutide (Xultophy®▼) should be recommended as an option for restricted use within NHS Wales. NMG were of the view that use should be restricted for a subpopulation within its licensed indication (for the treatment of adults with type 2 diabetes mellitus to improve glycaemic control in combination with oral glucose-lowering medicinal products when these combined with basal insulin do not provide adequate glycaemic control). NMG were of the view that insulin degludec/liraglutide (Xultophy®▼) should not be recommended for use within NHS Wales outside of this subpopulation as evidence to support use within the full licensed indication had not been provided. NMG suggested that insulin degludec/liraglutide (Xultophy®▼) should be prescribed by brand name to avoid medication errors.

The Chairman opened the discussion in relation to clinical effectiveness. Members sought clarification in relation to the study design. The Chairman drew attention to the clinical expert views. Dr Francis relayed the clinical expert view that insulin glargine is the most widely used insulin analogue in Wales and liraglutide is the most commonly used GLP-1 RA. Experts considered that insulin degludec has an advantage over insulin glargine in terms of lower risk of nocturnal hypoglycaemia. Xultophy®▼ would be considered in patients with T2DM who have suboptimal glycaemic control on basal analogue insulin where further reduction in HbA_{1c} would achieve their individualised target. Clinicians felt this would especially be the case where hypoglycaemia and weight gain might be problematic or could worsen.

The Chairman invited Professor Cohen to comment on the case for cost-effectiveness. Professor Cohen confirmed his role as AWMSG health economist and confirmed he had no involvement in compiling the ASAR or in discussions at NMG. Professor Cohen provided an overview of the case presented, as summarised in the ASAR, and offered the company delegates opportunity to correct or comment on any aspect of his summary.

The Chairman drew members' attention to the budget impact evidence in the ASAR. There was discussion in relation to Table 3 and a comment made that the applicant company's assumptions appeared conservative. The company delegate explained how the figures had been derived. Mrs Samuels confirmed that AWMSG appraises medicines on their current list price unless a patient access scheme has been provided.

The Chairman referred members to the three patient organisation questionnaires and confirmed that all members had received and read the documentation. For the purposes of transparency Mr Palmer was asked by the Chairman to highlight salient aspects of the patient questionnaires. It was noted that the once daily injection, ease of administration and improved side effect profile compared to insulin would offer benefits to patients. It was clarified that the medicine was available in one strength only, thereby reducing the likelihood of medication errors. The patient experiences were relayed by Mr Palmer and the improvements to quality of life noted. There were no outstanding wider societal issues.

The Chairman referred to the applicant company's response and offered further opportunity for the company delegate to comment prior to concluding the appraisal. The delegates thanked AWMSG and highlighted the added benefits that the medicine offered to patients, including simpler option and improved compliance. 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:

Insulin degludec/liraglutide (Xultophy®▼) is recommended as an option for restricted use within NHS Wales.

Insulin degludec/liraglutide (Xultophy®▼) is licensed for the treatment of adults with type 2 diabetes mellitus to improve glycaemic control in combination with oral glucose-lowering medicinal products when these alone or combined with a glucagon-like peptide protein-1 (GLP-1) receptor agonist or basal insulin do not provide adequate glycaemic control.

Insulin degludec/liraglutide (Xultophy®▼) is restricted for use in combination with oral glucose-lowering medicinal products when these combined with basal insulin do not provide adequate glycaemic control.

Insulin degludec/liraglutide (Xultophy®▼) is not recommended for use within NHS Wales outside of this subpopulation.

The Chairman informed members that Brancaster Pharma Ltd had requested a change to the schedule. It was confirmed that Boehringer Ingelheim Ltd had no objections to this request and agreed that the appraisal of midodrine hydrochloride (Bramox) could be undertaken next.

7. Appraisal 2: Full Submission

Midodrine hydrochloride (Bramox®) in adults for the treatment of severe orthostatic hypotension due to autonomic dysfunction when corrective factors have been ruled out and other forms of treatment are inadequate

The Chairman welcomed delegates from Brancaster Pharma Ltd.

The Chairman reminded members to declare any interests in either the applicant company or the medicine if they had not already done so. Mr Rob Thomas joined the meeting and no further interests were declared.

The Chairman referred to his previous statement regarding the impact of AWMSG advice on the licensed status of the technology and the inherent implications associated with this, and invited Ms Kelly Wood, the AWTTC Appraisal Lead, to set the context of the appraisal.

Ms Wood presented an overview of the submission as detailed in the ASAR. She highlighted that midodrine hydrochloride (Bramox®) is a branded generic and licensing was based on a bioequivalence study demonstrating equivalence to the European product, Gutron. It was noted that Bramox is the only medicine licensed for the treatment of severe orthostatic hypotension due to autonomic dysfunction in Wales. Ms Wood confirmed that a patient organisation questionnaire had been received from the Syncope Trust and Reflex Anoxic Seizures (STARS). Members were informed that the medicine is available in Scotland following a positive HTA by the SMC.

The Chairman invited Dr Saad Al-Ismail, the NMG Chairman, to provide a brief overview of the relevant issues identified in the preliminary appraisal. Dr Al-Ismail confirmed the view of NMG that midodrine hydrochloride (Bramox®) should be recommended for use within NHS Wales for the treatment of severe orthostatic hypotension due to autonomic dysfunction when correctable factors have been treated and other forms of treatment are inadequate. NMG suggested that the initiation and dose titration should be restricted to specialist prescribing.

The Chairman opened the discussion and members discussed issues relating to clinical effectiveness. The company delegate stated that the relatively small study was related to the

low frequency of the illness. The most common dose was confirmed as below 10mg tds. There was discussion over patient selection and the safety profile. Ms Wood highlighted the key aspects of the clinical expert summary. Clinical experts confirmed that unlicensed midodrine is in use within NHS Wales for the indication under consideration. In their opinion midodrine should be offered following education and support, aggressive lifestyle modification, increased fluid and electrolyte intake and fludrocortisone. It was noted that both fludrocortisone and ephedrine are used off label in the treatment of orthostatic hypotension. Members were informed that the clinical expert at NMG considered that once a patient had been initiated and stabilised on midodrine, repeat prescription by a specialist would not be required.

The Chairman invited Professor Cohen to comment on the case for cost-effectiveness. Professor Cohen confirmed his role as AWMSG health economist and confirmed he had no involvement in compiling the ASAR or in discussions at NMG. Professor Cohen summarised the case presented and offered the company delegates opportunity to correct or comment on any aspect of his summary. It was noted that the applicant company had submitted a cost minimization analysis based on the therapeutic equivalence of Bramox and unlicensed Midodrine. Professor Cohen alluded to the limitations of a cost minimization analysis. Members noted the budget impact estimates and the overall net cost savings estimated at £56K to £71K over the next five years. Professor Cohen highlighted the small quality of life improvements and questioned whether any treatment for this condition offered a good use of valuable NHS resources.

The Chairman confirmed that members had received and read the patient organisation submission and, in the interests of transparency, asked the lay member, Mr Chris Palmer, to highlight the salient issues. Mr Palmer relayed the patient view that treatment offered an opportunity for normality in their daily life as patients felt more confident and self-sufficient. It was suggested that treatment could enable a return to work, continuation of studies or return of a driving licence. Patients highlighted experience of lack of understanding of the havoc that syncope and postural orthostatic tachycardia syndrome can cause. Members noted that midodrine hydrochloride (Bramox®) may be supplied by a home healthcare provider for some patients. There were no other societal issues.

The Chairman referred to the company response to the preliminary recommendation and invited the company delegates to comment. Prior to concluding the appraisal proceedings he asked the company delegates to confirm they were satisfied that all issues had been adequately addressed and taken into account, and that the process had been fair and transparent. The company delegates provided confirmation and thanked Boehringer Ingelheim Limited for enabling the re-scheduling of the appraisals. The Chairman concluded the appraisal proceedings.

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:

Midodrine hydrochloride (Bramox®) is recommended for use within NHS Wales for the treatment of severe orthostatic hypotension due to autonomic dysfunction when corrective factors have been ruled out and other forms of treatment are inadequate.

Mr Rob Thomas left the meeting.

8. Appraisal 3: Full Submission
Tiotropium (Spiriva® Respimat®) indicated as add-on maintenance bronchodilator treatment in adult patients with asthma who are currently treated with the maintenance combination of

inhaled corticosteroids (≥800 micrograms budesonide/day or equivalent) and long-acting beta 2 agonists and who experienced one or more severe exacerbations in the previous year

The Chairman welcomed delegates from the applicant company, Boehringer Ingelheim Limited.

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 regarding the impact of AWMSG advice on the licensed status of the technology and confirmed that AWMSG advice would be interim to final NICE advice should this be subsequently published.

The Chairman outlined the sequence of events and invited Dr Caron Jones, AWTTC Appraisal Lead, to set the context of the appraisal. Dr Jones presented an overview of the submission as detailed in the ASAR. Dr Jones explained that in their submission, the company compared tiotropium plus usual care against usual care alone; there was no comparison with other treatment options at step four. Guidelines recognise that there are few clinical trials in this specific patient group and recommendations are largely based on extrapolation from trials of add-on therapy to ICS alone. Dr Jones confirmed that no patient organisation submissions had been received. It was noted that the medicine is available in NHS Scotland via HTA.

The Chairman invited Dr Saad Al-Ismail, the NMG Chairman, to provide a brief overview of the relevant issues identified in the preliminary appraisal. Dr Al-Ismail confirmed the view of NMG that tiotropium (Spiriva® Respimat®) should be recommended as an option for use within NHS Wales as an add-on maintenance bronchodilator treatment in adult patients with asthma who are currently treated with the maintenance combination of inhaled corticosteroids (≥ 800 micrograms budesonide daily or equivalent) and long-acting beta2 agonists and who experienced one or more severe exacerbations in the previous year.

The Chairman opened the discussion in relation to clinical effectiveness. There was discussion over the difference in effectiveness of the lung function results. Members sought clarification in relation to systematic differences in the group. Members asked the company delegates to provide their rationale for the choice of device. Members asked the company delegates to highlight any benefits in terms of reduced hospitalization or admittance to Accident and Emergency departments. The Chairman drew members' attention to the clinical expert summary. Dr Jones relayed the experts' view that treatment options were limited at steps 4 and 5. Experts considered there was a therapeutic gap and the availability of tiotropium as a treatment option would be advantageous. Experts highlighted that due to the diagnostic overlap between chronic asthma and chronic obstructive pulmonary disease, tiotropium has already been used in asthmatic patients. The uncertainty in estimating the number of patients eligible for treatment with NHS Wales was highlighted.

The Chairman invited Professor Cohen to comment on the case for cost-effectiveness. Professor Cohen confirmed his role as AWMSG health economist and confirmed he had no involvement in compiling the ASAR or in discussions at NMG. Professor Cohen summarised the case presented and offered the company delegates opportunity to correct or comment on any aspect of his summary. Professor Cohen highlighted the limitations and high level of uncertainty in the case for cost-effectiveness as presented in the ASAR. There was discussion over the uptake assumptions and concern was expressed over the mismatch in exacerbation rates within the evidence. Members noted the budget impact estimates and it was noted that the calculations take account of the additional acquisition costs of tiotropium and the cost savings from the avoidance of severe exacerbations.

Mr Chris Palmer highlighted the steps taken by AWMSG to seek input from a patient organisation. Asthma UK Cymru and the British Lung Foundation had been invited to submit

views but neither had responded to AWTTC's request for a patient organisation submission.

The Chairman referred to the company response to the preliminary recommendation and invited the company delegates to highlight aspects of their response. Prior to concluding the appraisal proceedings the Chairman asked the company delegates to confirm they were satisfied that all issues had been adequately addressed and taken into account, and that the process had been fair and transparent. On receipt of this confirmation he concluded the appraisal proceedings and members retired to vote on the three appraisals undertaken.

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:

Tiotropium (Spiriva® Respimat®) is not recommended for use within NHS Wales as an add-on maintenance bronchodilator treatment in adult patients with asthma who are currently treated with the maintenance combination of inhaled corticosteroids (≥ 800 micrograms budesonide daily or equivalent) and long-acting beta$_2$ agonists and who experienced one or more severe exacerbations in the previous year.

The company submission did not present sufficient evidence to demonstrate that tiotropium (Spiriva® Respimat®) is cost-effective, and there were uncertainties around the budget impact.

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded to all three applicant companies within five working days. He informed the 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.

Mr Rob Thomas rejoined the meeting

9. Appraisal 4 – Limited submission
Fosfomycin (Fomicyt®) for the treatment of the following infections in adults and children including neonates: acute osteomyelitis; complicated urinary tract infections; nosocomial lower respiratory tract infections; bacterial meningitis; and bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above

The Chairman welcomed delegates from Nordic Pharma UK Ltd

The Chairman reminded 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 confirmed that the application had been considered eligible for a limited submission and, in line with this process, evidence of budgetary impact against the existing comparator product should be demonstrated. The Chairman confirmed that if AWMSG makes a positive recommendation following appraisal of a limited submission, and it is subsequently ratified by Welsh Government, then monitoring budget impact would be essential. It was noted

that AWMSG reserves the right to request a full submission if the budget impact exceeded that estimated in a limited submission.

The Chairman outlined the sequence of events and invited Dr Caron Jones, AWTTC Appraisal Lead, to set the context of the appraisal. Dr Jones presented an overview of the submission as detailed in the ASAR.

Dr Jones explained that fosfomycin has been available in Europe for 40 years and is the first licensed version of intravenous fosfomycin available in the UK. In their submission, the applicant company highlighted that unlicensed fosfomycin was being imported for use in the UK and there is a need for a UK licensed intravenous fosfomycin preparation to eliminate uncertainty of supply and inconsistencies of documentation, formulation, presentation, handling and potential safety issues. It was noted that evidence was only provided for infections associated with MRSA, multidrug resistant Enterobacteriaceae and multidrug resistant *Pseudomonas aeruginosa.* Dr Jones clarified that the licensed indication states that fosfomycin should be used when alternative antibacterial agents have failed to demonstrate efficacy. Members were informed that no patient organisation submissions had been received.

The NMG Chairman, Dr Saad Al-Ismail, confirmed that NMG had supported the restricted use of fosfomycin (Fomicyt®) for use within its licensed indication for the treatment of infections in adults and children including neonates: acute osteomyelitis; complicated urinary tract infections; nosocomial lower respiratory tract infections; bacterial meningitis; and bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed. NMG advised that it should be prescribed by a specialist in infectious disease or under the guidance of a microbiologist.

Members expressed concern over the lack of evidence. The company delegate explained to members that they had made their best possible submission and acknowledged the paucity of data. The Chairman referred to the clinical expert views. It was noted that experts welcomed a new antibiotic to treat newly emergent multiresistant strains such as carbapenemase-producing Enterobacteriaceae and similar organisms, for which there are few, if any, other options. Mr Palmer confirmed that three patient organisations had been invited to submit views; however none had been received. There were no wider societal issues of note.

The Chairman referred to the company response to the preliminary recommendation and invited the company delegates to highlight aspects of their response. Prior to concluding the appraisal proceedings the Chairman asked the company delegates to confirm they were satisfied that all issues had been adequately addressed and taken into account, and that the process had been fair and transparent. On receipt of this confirmation he concluded the appraisal proceedings and members retired to vote on the three appraisals undertaken.

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:

Fosfomycin (Fomicyt®) is recommended as an option for use within NHS Wales for the treatment of the following infections in adults and children including neonates: acute osteomyelitis; complicated urinary tract infections; nosocomial lower respiratory tract infections; bacterial meningitis; and bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above.

Fosfomycin (Fomicyt®) should be used only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the initial treatment of the infections listed above, or when these alternative antibacterial agents have failed to

demonstrate efficacy.

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded to applicant companies within five working days. He informed the 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.

10. Appraisal 5 – Limited Submission

Travoprost (Travatan®) for the decrease of elevated intraocular pressure in paediatric patients aged 2 months to < 18 years with ocular hypertension or paediatric glaucoma

The Chairman welcomed delegates from Alcon Laboratories (UK) Ltd

The Chairman reminded 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 confirmed that the application had been considered eligible for a limited submission and, in line with this process, evidence of budgetary impact against the existing comparator product should be demonstrated. The Chairman confirmed that if AWMSG makes a positive recommendation following appraisal of a limited submission, and it is subsequently ratified by Welsh Government, then monitoring budget impact would be essential. It was noted that AWMSG reserves the right to request a full submission if the budget impact exceeded that estimated in a limited submission.

The Chairman outlined the sequence of events and invited Dr Claire Davis, AWTTC Appraisal Lead, to set the context of the appraisal. Dr Davis presented an overview of the submission as detailed in the ASAR. Dr Davis clarified that a limited submission was considered appropriate for this paediatric licence extension with minor budgetary impact. It was noted that the medicine is available via HTA within NHS Scotland. Dr Davis confirmed that no patient organisations submissions had been received.

The Chairman invited Dr Saad Al-Ismail to relay the views of NMG. Dr Al-Ismal confirmed NMG's preliminary recommendation that travoprost (Travatan®) should be available as an option for use within NHS Wales for the decrease of elevated intraocular pressure in paediatric patients aged 2 months to < 18 years with ocular hypertension or paediatric glaucoma.

The Chairman opened the discussion. Members sought clarification in relation to the choice of comparator. No areas of unmet need in relation to this condition had been highlighted by clinical experts. The company delegates confirmed there is very little difference in the safety profile compared with the comparator. A discrepancy in relation to number of eligible patients was noted. The Chairman referred members to the views of clinical experts – there were no outstanding issues to note. Mr Palmer confirmed that the Royal National Institute of Blind People and the Eyecare Trust had declined to make a patient organisation submission. There were no wider societal issues of note.

The Chairman referred to the company response to the preliminary recommendation and invited the company delegates to highlight aspects of their response. Prior to concluding the

appraisal proceedings the Chairman asked the company delegates to confirm they were satisfied that all issues had been adequately addressed and taken into account, and that the process had been fair and transparent. On receipt of this confirmation he concluded the appraisal proceedings and members retired to vote on the two appraisals undertaken.

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:

Travoprost (Travatan®) is recommended as an option for use within NHS Wales for the decrease of elevated intraocular pressure in paediatric patients aged 2 months to < 18 years with ocular hypertension or paediatric glaucoma.

The Chairman announced that confirmation of AWMSG's recommendations would be forwarded to applicant companies 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 Chairman confirmed the date of the next meeting on **Wednesday, 11th November 2015 in Cardiff** and closed proceedings.