Enclosure No:	**1/AWMSG/0216**
Agenda Item No:	**1** – Minutes of previous meeting
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ALL WALES MEDICINES STRATEGY GROUP (AWMSG)

Draft minutes of the AWMSG meeting held
Wednesday 9th December 2015 commencing 9.30 am
at the Angel Hotel, Abergavenny, NP7 5EN

VOTING MEMBERS PRESENT:			**Did not participate in**
1.	Dr Stuart Linton	Chair	
2.	Professor John Watkins	Public Health Wales / Vice Chair	
3.	Dr Catherine Bale	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	**8, 9**
9.	Mrs Ellen Lanham	Community Pharmacist	
10.	Mrs Alison Hughes	Managed Sector Primary Care Pharmacist	
11.	Mr Christopher Palmer	Lay Member	
12.	Mr Bill Malcolm	ABPI Cymru Wales	**8, 9**
13.	Mr John Terry	Managed Sector Secondary Care Pharmacist	

WELSH GOVERNMENT:
Professor Roger Walker, Chief Pharmaceutical Officer (for agenda items 10-12)

IN ATTENDANCE:
Mr Scott Pegler, NMG Vice Chair
Mr Anthony Williams, Senior Appraisal Pharmacist (Team Leader), AWTTC
Mrs Ruth Lang, Head of Liaison & Administration, AWTTC

AWTTC APPRAISAL LEADS:

Mr Anthony Williams, Senior Appraisal Pharmacist
Mrs Sue Cervetto, Senior Appraisal Pharmacist
Mrs Gail Woodland, Senior Appraisal Pharmacist
Ms Kelly Wood, 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

Mr Scott Cawley (Other professions eligible to prescribe)
Dr Emma Mason & Dr Balwinder Bajaj (Clinical Pharmacologist)
Dr Mark Walker & Dr Brendan Boylan (Medical Director)
Mrs Louise Williams & Mrs Mandy James (Senior Nurse)

3. Declarations of interest

The Chairman invited declarations of interest pertinent to the agenda. Mr Bill Malcolm declared a personal specific interest in relation to appraisal 2 and 3 – he is employed by Bristol Myers Squibb. The Chairman confirmed that Mr Malcolm would not participate in the appraisal or vote.

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 October meeting. AWTTC had informed the Service on 20th November of the following advice:

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.

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.

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.

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 reported that following receipt of the negative recommendation in relation to tiotropium (Spiriva®Respimat®), the marketing authorisation holder, Boehringer Ingelheim Limited, requested an independent review (IR). The Chairman agreed that an Independent Review panel will be convened in the New Year to explore Boehringer's complaint in relation to misinterpretation of information. The panel will report back to AWMSG following that meeting.

The Chairman announced the statements of advice that had been ratified by Welsh Government and uploaded to the AWMSG website. He confirmed the medicines are not endorsed for use within NHS Wales.

Evolocumab (Repatha®) for the treatment of adults and adolescents aged 12 years and over with homozygous familial hypercholesterolaemia in combination with other lipid-lowering therapies.

Golimumab (Simponi®) for the treatment of adults with severe, active non radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C reactive protein and/or magnetic resonance imaging evidence, who have had an inadequate response to, or are intolerant to nonsteroidal anti-inflammatory drugs.

Ibrutinib (Imbruvica®) for the treatment of adult patients with Waldenstrom's macroglobulinemia who have received at least one prior therapy, or in first line treatment for patients unsuitable for chemo-immunotherapy.

Perampanel (Fycompa®) for the adjunctive treatment of primary generalised tonic-clonic seizures in adult and adolescent patients from 12 years of age with idiopathic generalised epilepsy.

Pertuzumab (Perjeta®) in combination with trastuzumab and chemotherapy for the neoadjuvant treatment of adult patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer at high risk of recurrence.

Sapropterin (Kuvan®) for the treatment of hyperphenylalaninaemia (HPA) in adults and paediatric patients of all ages with phenylketonuria (PKU) who have been shown to be responsive to such treatment; or for the treatment of hyperphenylalaninaemia (HPA) in adults and paediatric patients of all ages with tetrahydrobiopterin (BH4) deficiency who have been shown to be responsive to such treatment.

The Chairman thanked those from the pharmaceutical industry who had attended the AWMSG Masterclass held on 25th November 2015 to learn more about the appraisal process and how to make a good submission. Members were informed that feedback from the meeting had been extremely positive and was very welcome.

The Chairman referred to his announcement at the previous meeting that Professor David Cohen and Dr Geoffrey Carroll were retiring and this would be their last AWMSG meeting. The Chairman passed on his personal thanks, and those of the Committee, for the outstanding contribution of Professor Cohen and Dr Carroll to the work of AWMSG over many years. The Chairman announced the retirement of Professor Roger Walker, Chief Pharmaceutical Officer and thanked him for his support of AWMSG. The Chairman announced the resignation of Mr Alun Morgan representing other professions eligible to prescribe.

The Chairman announced the appraisals scheduled for the next AWMSG meeting on

Wednesday, 24th February 2016 in Abergavenny.

Pasireotide (Signifor®) 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
Applicant Company: Novartis Pharmaceuticals UK Ltd

Ivermectin (Soolantra®) for the treatment of inflammatory lesions of rosacea (papulopustular) in adult patients
Applicant Company: Galderma (UK) Ltd

Oseltamivir (Tamiflu®) for the treatment of infants less than 1 year of age including full term neonates who present with symptoms typical of influenza, when influenza virus is circulating in the community. Efficacy has been demonstrated when treatment is initiated within two days of first onset of symptoms
Applicant Company: Roche Products Ltd

Ustekinumab (Stelara®) for the treatment of chronic moderate to severe plaque psoriasis in adolescent patients from the age of 12 years and older, who are inadequately controlled by, or are intolerant to, other systemic therapies or phototherapies
Applicant Company: Janssen-Cilag 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. All Wales Syringe Driver Chart

The Chairman invited Mrs Elizabeth Lewis, Palliative Care Pharmacist in Hywel Dda Health Board to present Enc 2/AWMSG/1215, an All Wales Syringe Driver Chart. Mrs Lewis explained that the Welsh Palliative Care Pharmacists Group had collated information on how syringe drivers were being prescribed across Wales. It had been noted that practice varied greatly and in order to reduce variability and promote safer prescribing, a single chart had been developed for use in all settings. The All Wales syringe driver chart had been developed through the framework set out by the All Wales Quality and Safety sub-group of the Drug Chart Reference Group. A task and finish group had been formed with representation from each health board and there had been wide consultation during the development of the chart. To assist with the implementation of the chart a powerpoint presentation and an instruction guide had been developed. Subject to endorsement by AWMSG, it is intended that the chart, the presentation and instruction guide would be available on the AWMSG website.

The Chairman opened discussion and members welcomed the chart and accompanying resources. Members sought clarification in relation to implementation and Mrs Lewis confirmed that each health board would be responsible for local implementation. A suggestion was made to include the out-of-hours service and district nurses. Mrs Lewis confirmed that district nurses had been involved in the development of the chart. Dr Black suggested that it would be helpful to include the NHS number as well as the health record number on the chart. Mrs Lewis reassured members that the chart would cross over the interface between secondary and primary care. There was discussion around the continuous use section. Members supported the development of the chart and considered it to be a significant step towards improved quality and patient safety. The Chairman closed discussion by confirming AWMSG's endorsement of the chart and supporting information.

7. Appraisal 1: Full Submission

Empagliflozin (Jardiance®) for the treatment of type 2 diabetes mellitus to improve glycaemic control in adults as monotherapy when diet and exercise alone do not provide adequate glycaemic control in patients for whom use of metformin is considered inappropriate due to intolerance

The Chairman welcomed representation from 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 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 Mrs Gail Woodland, AWTTC Appraisal Lead, to set the context of the appraisal.

Mrs Woodland presented an overview of the submission as detailed in the ASAR. The Chairman invited Mr Scott Pegler to provide a brief overview of the relevant issues identified in the preliminary appraisal by NMG. Mr Pegler confirmed that at their meeting on 4th November 2015, NMG had recommended this medicine as an option for use within NHS Wales for the indication being appraised.

The Chairman opened the discussion in relation to clinical effectiveness. Members sought clarification in relation to the adverse effect profile. There was discussion over the FDA warning in relation to diabetic ketoacidosis. Members were assured that the marketing authorisation holders, Boehringer Ingelheim Ltd, were undertaking a pharmacovigilance assessment. Mrs Woodland relayed the views of the clinical experts as summarised in the enclosure. Experts highlighted that reduction in cardiovascular disease (CVD) was a major unmet need for all therapies which lower blood glucose levels in people with T2DM and commented on the recent findings of the EMPA-REG study though it was noted that the vast majority of patients in this study were on combination therapy. The niche identified by the clinical experts was noted.

The Chairman invited Professor Cohen to comment on the case for cost-effectiveness. Professor Cohen confirmed his role as AWMSG health economist and assured the company delegates that he had no involvement in compiling the ASAR or 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. There were no specific issues of note other than a comment that dominance may have been overstated.

The Chairman drew members' attention to the budget impact evidence in the ASAR. The relatively modest impact on market share compared with the competitor medicines was noted. There was discussion in relation to the comparators and perceived clinical benefit. There was also discussion in relation to the eligible patient population.

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 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 received from Diabetes UK Cymru. Mr Palmer relayed the view that this treatment had been shown to have positive effects on weight management. In addition,

new evidence recently published had indicated that people taking empaglifozin had significantly lower rates of death from cardiovascular causes, hospitalization for heart failure and death from any cause. The disadvantages to treatment were also highlighted – increased risk of genital infection and thrush, potential risk of kidney failure and diabetic ketoacidosis. The importance of having a range of treatment options available was noted. There were no other wider societal issues of note.

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 delegate offered some closing remarks. 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:

Empagliflozin (Jardiance®▼) is recommended as an option for the treatment of type 2 diabetes mellitus to improve glycaemic control in adults as monotherapy when diet and exercise alone do not provide adequate glycaemic control in patients for whom use of metformin is considered inappropriate due to intolerance.

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.

Mr Bill Malcolm left the meeting. Dr Karen Fitzgerald left the meeting.

8. Appraisal 2: Limited Submission

Efavirenz (Sustiva®) indicated in antiviral combination treatment of human immunodeficiency virus-1 (HIV-1) infected children 3 months of age and weighing at least 3.5 kg to children 3 years of age

The Chairman welcomed representation from the applicant company, Bristol-Myers Squibb Pharmaceuticals Limited.

The Chairman reminded 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 and the Chairman confirmed that Mr Malcolm had left the room.

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.

Mrs Cervetto presented the ASAR and the Chairman asked members if there were any issues in the ASAR requiring further discussion or clarification. Members sought clarification in relation to the estimated number of eligible patients. It was confirmed that no patient organisation submission had been received despite an approach by AWTTC to a number of organisations. Mrs Cervetto relayed the clinical expert view and the Chairman referred members to the summary included in the meeting papers. The Chairman invited the applicant company delegates to address the group. 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:

Efavirenz (Sustiva®) is recommended as an option for use within NHS Wales in antiviral combination treatment for the treatment of human immunodeficiency virus-1 (HIV-1) infected children 3 months of age to 3 years and weighing at least 3.5kg.

Sustiva® has not been adequately studied in patients with advanced HIV disease, namely patients with CD4 counts < 50 cells/mm^3, or after failure of protease inhibitor (PI) containing regimens. Although cross-resistance of efavirenz with PIs has not been documented, there are at present insufficient data on the efficacy of subsequent use of PI based combination therapy after failure of regimens containing Sustiva®.

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.

9. Appraisal 3 – Limited Submission
Atazanavir/cobicistat (Evotaz®▼) in combination with other antiretroviral medicinal products for the treatment of HIV-1 infected adults without known mutations associated with resistance to atazanavir

The delegates from the applicant company, Bristol-Myers Squibb Pharmaceuticals Limited, remained seated. The Chairman reminded 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 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 AWTTC appraisal lead, Ms Kelly Wood, presented an overview of the submission as critiqued in the ASAR. The Chairman asked members if there were any issues in the ASAR requiring further discussion or clarification. There were none. It was confirmed that no patient organisation submission had been received. Ms Wood relayed the views of the clinical experts and the Chairman referred members to the summary included in the meeting papers. It was highlighted that atazanavir is used only as an alternative option when other treatments are not suitable.

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 had no further comment. 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:

Atazanavir/cobicistat (Evotaz®▼) in combination with other antiretroviral medicinal products is recommended as an option for use within NHS Wales for the treatment of HIV-1 infected adults without known mutations associated with resistance to atazanavir.

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 closed the meeting to members of the public and confirmed that in order to protect commercial confidentiality the next three appraisals would be conducted in private as the submissions included an associated Wales patient access scheme.

Professor Roger Walker joined the meeting. Mr Bill Malcolm and Dr Karen Fitzgerald returned.

10. Appraisal 4 – Full Submission (WPAS)

Macitentan (Opsumit®) as monotherapy or in combination, for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients of WHO Functional Class (FC) II to III

The Chairman welcomed representation from Actelion Pharmaceuticals UK Limited. The Chairman confirmed that members of the public had vacated and individuals remaining in the meeting room were associated with AWTTC.

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

Mrs Cervetto presented an overview of the submission as detailed in the ASAR. Mr Scott Pegler confirmed that NMG had appraised the medicine on 4th November and had recommended macitentan (Opsumit®) as an option for use within NHS Wales as monotherapy, or in combination, for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients of WHO Functional Class (FC) II to III.

The Chairman opened the discussion and members highlighted issues relating to clinical effectiveness. The company was commended on the size of the study. It was noted that the company were not making the case for clinical superiority; however the adverse event profile appeared to be dominant over the comparator. There was discussion in relation to the future service model for pulmonary hypertension in that patients living in Wales would be managed locally. There were no clinical expert views available.

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 highlighted the limitations of the cost minimisation analysis. The high levels of uncertainly in the assumptions were noted. The Chairman referred to the budget impact estimates and clarification was sought in relation to the number of eligible patients in Wales. Mr Palmer confirmed that three patient organisations had been approached but none had submitted views. Mr Palmer highlighted the reduced rate of adverse reactions and welcomed additional treatment options for clinicians.

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 had no further comment and thanked AWMSG for their assessment. 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:
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:

Macitentan (Opsumit®▼) is recommended as an option for use within NHS Wales as monotherapy or in combination for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients of WHO Functional Class (FC) II to III. This recommendation applies only in circumstances where the approved Wales Patient Access Scheme is utilised.

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.

11. Appraisal 5 – Full Submission (WPAS)

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

The Chairman welcomed representation from the applicant company, Merck Serono Limited.

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

Mr Tony Williams presented an overview of the submission as detailed in the ASAR. Mr Pegler relayed the view of NMG that the medicine for the indication appraised should not be recommended for use within NHS Wales as the case for cost-effectiveness had not been proven. NMG considered that AWMSG's criteria for appraising life-extending, end-of-life medicines were not applicable in this case. It was explained that having received the negative preliminary appraisal recommendation the applicant company had requested a meeting to explore issues in relation to AWMSG's policy for appraising life-extending, end of life medicines. A panel meeting had been convened on 4th November, Chaired by Dr Robert Bracchi. Dr Bracchi confirmed that having assessed the evidence, the panel had agreed with NMG and concluded that there was insufficient evidence that the cumulative population of each licensed indication of the medicine was small and, as such, did not conform to AWMSG's end of life policy. Mr Williams confirmed that the medicine is currently available to patients living in Scotland via HTA and in England via the Cancer Drug Fund (CDF). A review of NICE TA 176 is anticipated in April 2016. It was noted that in the absence of evidence for one component of the licensed indication (use as a single agent in patients who have failed oxaliplatin- and irinotecan-based therapy and who are intolerant to irinotecan) that use in this indication could not be discussed or supported.

The Chairman opened the discussion and members discussed issues relating to clinical effectiveness. Members sought clarification in relation to the patient population and Dr Bale offered her experience of clinical practice. Members discussed potential use in a sub-population highlighted by experts as an unmet need as treatment options are limited. There was discussion over the dosing regimen that would be used in routine clinical practice in Wales. The company delegates urged members to take a pragmatic approach as, in their opinion, in clinical practice the number of eligible patients in Wales would be lower than anticipated in the submission. Dr Bale concurred with this view and highlighted the need for Welsh patients to be included in future clinical trials. The Chairman referred to the clinical expert summary and Mr Williams relayed the experts' views.

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.

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 joint submission on behalf of Beating Bowel Cancer and Bowel Cancer UK 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 organisation questionnaire. Mr Palmer highlighted the huge psychological impact on the patient and their family when a diagnosis of advanced bowel cancer has been received, and the importance of reassuring patients that they

have access to the best known and clinically effective treatments. He referred to the evidence from patients indicating that targeted therapies have significant potential to improve survival and quality of life. He also stated the importance of having immediate access to treatments which offered the best possible outcome.

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 had no further comment. 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:
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:

Cetuximab (Erbitux®) is recommended as an option for restricted use within NHS Wales for the first-line treatment of patients with epidermal growth factor receptor (EGFR)-expressing, RAS wild-type metastatic colorectal cancer in combination with irinotecan-based chemotherapy or in combination with FOLFOX. This recommendation applies only in circumstances where the approved Wales Patient Access Scheme is utilised.

Cetuximab (Erbitux®) is not recommended for use within NHS Wales for the treatment of patients with EGFR-expressing, RAS wild-type metastatic colorectal cancer as a single agent in patients who have failed oxaliplatin- and irinotecan-based therapy and who are intolerant to irinotecan.

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 from the meeting 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.

12. Appraisal 6 – Full Submission (WPAS)

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 Chairman welcomed representation from the applicant company, Vertex Pharmaceuticals Limited.

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

Mrs Gail Woodland presented an overview of the full submission as detailed in the ASAR. Members were informed that the medicine for the licence extension is available in England via

a commissioning arrangement and also in NHS Scotland although there are currently no eligible patients. Mrs Woodland highlighted the issue of inequity of access currently within NHS Wales for patients with these gene mutations.

Mr Pegler provided a brief overview of the relevant issues identified in the preliminary appraisal and relayed the view of NMG that the medicine, for the indication being appraised, should not be routinely available for use within NHS Wales because the case for cost-effectiveness had not been proven. The view of NMG was that there were several uncertainties and limitations in the economic model provided in the company's submission. Mr Pegler confirmed that NMG agreed the medicine satisfies the AWMSG criteria for ultra-orphan drug status.

The Chairman opened the discussion and members discussed issues relating to clinical effectiveness. Dr Carroll explained the role of WHSSC in developing the clinical access policy for cystic fibrosis patients in Wales, which included the monitoring and review of clinical outcomes. The company delegate commented that the results from the clinical trial were ground-breaking and that there is similarity in treatment efficacy for this patient group of patients to that of patients with the G155D mutation. The Chairman referred to the clinical expert summary. It was noted that ivacaftor is a first in class medication and is the only therapy that targets and acts at the underlying pathology. All other existing treatments aim at alleviating disease consequences. While standard care does not currently include ivacaftor, experts stated that their preferred treatment would be to commence all patients with a class III CFTR mutation on ivacaftor. The unmet needs were highlighted by the clinical experts and relayed by Mrs Woodland. Members sought clarification in relation to the trial data and the intervariability in clinical outcome was highlighted by the company delegate.

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. The company delegate commended Professor Cohen on his summary. There was discussion in relation to the budget impact and clarification was sought in relation to the price offered to NHS Wales via the WPAS. The company delegate confirmed that the price offered to NHS Wales was the same as the rest of the UK. Mr Davies sought confirmation that Wales would be offered a fair deal compared to the rest of the UK. The company delegate confirmed this to be the case and highlighted that Vertex has been open to discussion from February and moving forward to ensure that the financial impact on NHS Wales is fair and equitable. There was agreement between the company delegate and AWMSG that this would be followed up and rigorously applied and any disparity would be pertinent to any decision made by AWMSG. Mr Stuart Davies highlighted the importance of equity across the UK in relation to the financial impact of this medicine on the NHS. The Chairman confirmed that a positive recommendation by AWMSG would be conditional on parity across the whole of the NHS.

Members were informed that following receipt of NMG's preliminary recommendation, Vertex Pharmaceuticals had requested a meeting of the newly formed Clinical and Patient Involvement Group (CAPIG) to further explore the benefits of this treatment for patients and their families/carers. The CAPIG Chairman, Dr Robert Bracchi, presented the CAPIG summary. It was noted that patients with G551D are currently receiving treatment with ivacaftor in Wales and the application under consideration covered the additional mutations which clinicians indicated represents an additional small number of patients in Wales. The Chairman asked the lay member, Mr Chris Palmer to comment. Mr Palmer confirmed his attendance at the CAPIG meeting and stated that the clinical experts in attendance had extolled the medicine. Mr Palmer referred to the patient organisation submission and highlighted the advantages of the treatment in that it offers an easy to administer oral therapy which improves lung function and offers hope for the future for patients with cystic fibrosis and their families. Mr Palmer stated that ivacaftor has been transformational and life-changing for a number of patients and is currently the only intervention that impacts positively on life

expectancy other than lung transplant. Patients report a vast improvement in lung function, appetite, weight and mental health, which translates positively to carers and other members of the family. Mr Palmer highlighted that inequitable access in relation to gene mutations would be unacceptable to patients living in Wales and he read a patient story.

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 delegate had no further comment. 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:
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:

Ivacaftor (Kalydeco®▼) is recommended for use within NHS Wales 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 CF transmembrane conductance regulator (*CFTR)* gene: *G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N,* or *S549R*. This recommendation applies only in circumstances where the approved Wales Patient Access Scheme is utilised.

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, 24th February 2016 in Abergavenny** and closed appraisal proceedings.